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# E. MERCK'S ANNUAL REPORT

:: OF RECENT ADVANCES IN ::  
PHARMACEUTICAL CHEMISTRY  
:: : AND THERAPEUTICS :: ::



1910 :: VOLUME XXIV :: DARMSTADT, JULY 1911.



THE HISTORY OF THE  
CITY OF BOSTON

FROM THE FIRST SETTLEMENT  
TO THE PRESENT TIME  
BY NATHANIEL BENTLEY



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E. MERCK, CHEMICAL WORKS, DARMSTADT 1911.



## Contents.

	Page
The Cacodylates and their Therapeutic Uses . . . . .	1—38
Kephir . . . . .	39—63
Preparations and Drugs . . . . .	64—380
Bibliographical Index . . . . .	381—389
Index of Authors . . . . .	390—405
General Index . . . . .	406—409
Index of Diseases, Symptoms and Indications for Treatment . . . . .	410—419



## The Cacodylates and their Therapeutic Uses.

The naturally occurring compounds of arsenium, particularly white arsenic, have always played a rather important rôle in the treatment of various skin diseases, and as cosmetics. It has remained for the investigators of the last hundred years to throw more light on the physiological mode of action of arsenium and of its derivatives. With the gain in our knowledge of the therapeutic value of arsenium compounds, the ill effects of arsenic treatment were also brought to light, and it was shown that the successful treatment of obstinate skin diseases requires the use of such considerable doses of the inorganic arsenic preparations as to produce appreciable injury to the organism as a whole, or to special parts of it. Thus among the secondary effects following the use of arsenic many cases have been observed\*) of changes in the skin, such as dermatitis, erythema, pigmentation and shedding of hair, also affections of the internal organs, including the mucous membrane of the throat, nose and eyes, also frequent disturbances of the kidneys and of the central nervous system. An attempt was consequently made to use organic compounds of arsenium, and by their agency to administer large and effective doses of arsenium, practically free from any toxic action; this was achieved by the use of the salts of cacodylic acid. These salts quickly took a firm place in therapeutics, and they have held their ground in spite of the introduction of newer preparations of arsenium, for they rarely produce any harmful secondary effects, nor do they subject the patient to the risk of dangerous permanent injury, such as complete blindness, as has been observed to follow the use of other organic compounds of arsenium.

The chemistry of the cacodylates and of cacodyle was fully studied by Bunsen. He found (1837) that the so-called Cadet's fluid (alkarsin), first prepared by Cadet (1760) by the distillation of arsenic with potassium acetate, consisted

\*) Lewin, Nebenwirkungen der Arzneimittel 1899, p. 358—372.

Bunsen, Liebig's Annalen XXIV, p. 271, XXVII, p. 148 (Dumas), XXXI, p. 175, XXXVII, p. 1, XXXXII, p. 14, XXXXVI, p. 1.

principally of cacodyle\*),  $\text{As}_2(\text{CH}_3)_4$  and of cacodyle oxide,  $\text{As}_2(\text{CH}_3)_4\text{O}$ . By oxidising these substances he then obtained cacodylic acid, which was distinguished from the substances out of which it was made chiefly by the absence of odour, and by its relative freedom from poisonous action.

At the present time the following preparations of cacodylic acid are on the market\*\*).

#### Acidum cacodylicum.

The free acid, also called dimethylarsinic acid, forms white crystals of the chemical composition  $(\text{CH}_3)_2\text{AsO} \cdot \text{OH}$ . It melts at  $200^\circ\text{C}$ . and is readily soluble in water and alcohol. For therapeutic purposes it is only used in exceptional cases, its sodium salt being commonly employed.

#### Sodii cacodylas.

Sodium cacodylate,  $(\text{CH}_3)_2\text{AsO} \cdot \text{ONa} + 3\text{H}_2\text{O}$ , is the most commonly used salt of cacodylic acid. It forms a white crystalline powder, very readily soluble in water. Its use and dosage are described in detail below.

#### Potassii cacodylas.

Potassium cacodylate,  $(\text{CH}_3)_2\text{AsO} \cdot \text{OK} + 2\text{H}_2\text{O}$ , forms white crystals, soluble in water, less soluble in alcohol. It may be used in the same way and in the same doses as the sodium salt.

#### Ferri cacodylas.

Cacodylate of iron,  $[(\text{CH}_3)_2\text{AsO} \cdot \text{O}]_3\text{Fe}$ , a yellowish powder, soluble in water, particularly in hot water. Its use is described below.

#### Quininæ cacodylas.

$\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_2(\text{CH}_3)_2\text{AsOOH}$ . This preparation forms a white powder, soluble in water and alcohol. It is said to be particularly well suited for the treatment of malaria

\*) The word "cacodyle" is derived from *κακός* and *ὀδὴς* (bad smell).

\*\*) For other salts of cacodylic acid, e. g. those of silver, barium, calcium, codeine etc., see:

Siboni, Bollettino chimico farmaceutico 1902, Vol. 41, p. 73.

Annoni, Bollettino chimico farmaceutico 1904, Vol. 44, p. 485.

Barthe and Minet, Comptes rendus de l'académie des sciences, Vol. 148, p. 1609.



and of syphilis. The dose for internal and subcutaneous use may be assumed to range between 0.1 and 0.25 gramme ( $1\frac{1}{2}$ —4 grains) though it has not yet been accurately determined. 1 gramme (15 grains) of cacodylate of quinine corresponds to 0.27 gramme ( $4\frac{1}{6}$  grain) of cacodylic acid, or to 0.426 gramme ( $6\frac{1}{3}$  grains) of sodium cacodylate.

#### Guaiacol cacodylas.

The preparation is a mixture, in molecular proportions, of guaiacol and cacodylic acid,  $C_6H_4(OH)OCH_3 + (CH_3)_2AsO.OH$ . It forms a white or reddish-white crystalline powder, soluble in alcohol, in fatty oils and in hot water. (For use and dosage see below.)

#### Hydrargyri cacodylas.

Mercuric cacodylate forms a white crystalline powder, soluble in water, of the composition  $[(CH_3)_2AsO_2]_2Hg$ . Its use in syphilis is described below. Since pure mercuric cacodylate is unstable, has an acid reaction and, according to Brocq and other authors is said to produce local inflammation when used subcutaneously, I issue under the name of "Hydrargyri cacodylas", not the simple salt, but a double salt of the above-named compound with sodium chloride. It contains 23 p.c. of oxide of mercury, and dissolves in water to a somewhat turbid fluid with a slightly alkaline reaction. (It corresponds approximately to the formula  $[(CH_3)_2AsO_2]_2Hg + 8NaCl$ ).

#### Lithii cacodylas.

$(CH_3)_2AsO.Li$ , is a white powder, soluble in water. It may be used in the same way and in the same doses as the sodium salt. No special indications for the use of this preparation have as yet been ascertained.

#### Magnesii cacodylas.

$[(CH_3)_2AsO.O]_2Mg + 2H_2O$  is a white powder, soluble in water. Its use is described below.

#### Manganesii cacodylas.

$[(CH_3)_2AsO.O]_2Mn$  is a reddish-white powder, soluble in water. It may be used in the same way as iron cacodylate.

Strychninæ cacodylas is a white salt, sparingly soluble in water.

Bunsen, Kürschner, as well as Schmidt and Chomse, ascertained by animal experiment the complete non-toxicity of cacodylic acid and of its salts. The last named two authors acknowledge that there might be some poisonous action under conditions which were not accurately known, for instance, in conditions of the intestines which may cause a transformation, i. e., a reduction of the cacodylic acid to cacodyle oxide. The poisonous action thus produced was thought by them to be due not to arsenium, but to a local irritant effect. Lebahn and Schulz found, however, that cacodylic acid produced a decided arsenium action, and that therefore it was a poisonous substance. Its toxicity, however, was materially less than that of arsenious acid. This view was accepted by Rabuteau as a result of his experiments, for he found that 2 grammes (30 grains) of cacodylic acid were required to poison a dog. J. Marshall and W. D. Green, however, who found that a dose of 3 grammes (45 grains) was required to kill a dog weighing 5 kilogrammes, incline more to Bunsen's view and are of opinion that cacodylic acid, when really free from white arsenic, has little or no poisonous action. The careful pharmacological investigations of these authors proved that cacodylic acid was less poisonous than arsenious acid. This cannot be attributed to the smaller amount of arsenium it contains (1 gramme [15 grains] of cacodylic acid corresponds to about 0.7 gramme [ $10\frac{3}{4}$  grains] of arsenious acid), for in practice, doses were subsequently given which contained 10 to 50 times the maximum dose of white arsenic. As to the fate of cacodylic acid in the organism they gave no clue, and at the present day we have no definite information on this point. It is commonly assumed that cacodylic acid

Bunsen-Kürschner, Liebigs Annalen Vol. XLVI., p. 1.

Schmidt - Chomse, Moleschotts Untersuchungen zur Naturlehre 1860, p. 122.

Lebahn, Dissertation Rostock 1868.

Schulz, Berichte der chemischen Gesellschaft Berlin 1879, Vol. XII., p. 22.

Rabuteau, Comptes rendus de la société de biologie 1882, p. 443.

Marshall-Green, American Medical Journal 1886, Vol. VIII., p. 128.



can only act if it is transformed in the organism into arsenious acid or arsenic acid. It is quite conceivable, however, that the unaltered molecule of cacodylic acid may produce a specific physiological action similar to that of arsenic. Quite recently this view has been advanced by Weland er with regard to atoxyl. The great therapeutic success of cacodylic acid treatment would be better explained by this assumption than by the results to be quoted presently of the physiological and pharmacological work which led to the conclusion that cacodylic acid possessed a limited therapeutic value.

Thomas R. Fraser, in his experiments on man with cacodylic acid and with sodium cacodylate, was unable to detect any arsenium action, either on internal or subcutaneous administration. He found further that cacodylic acid left the organism unchanged. In his opinion the arsenium is too firmly bound in the cacodyle molecule, and is thus prevented from exerting its action. This result agrees in some respects with those of Schmidt and Chomse, though not with those of Lebahn and Schulz. It is also partly in opposition to the results of Heffter's experiments. Heffter also assumes, however, that the action of cacodylic acid is probably due to the liberation of arsenium, and that the action is proportional to the amount of arsenium set free. He was able to demonstrate that a small part of the arsenium is actually split off from the organic combination, and appears in the urine as arsenious acid. He also showed that certain animal organs, such as the liver, intestine and the wall of the stomach, had the power of reducing cacodylic acid. Consequently, when cacodylates are given internally, the odour of oxide of cacodyle occurs, while this phenomenon very rarely follows their subcutaneous exhibition. Heffter therefore gave preference to the subcutaneous method of application, and further experience has endorsed this attitude, the subcutaneous exhibition of these

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Weland er, *Hygiea* 1909, p. 97, *Nordisches medizinisches Archiv* 1909, II., No. 3, p. 27.

Fraser, *Scottish Medical and Surgical Journal* 1902, May, *British Medical Journal* 1902, No. 2151, p. 712.

Heffter, *Archiv für experimentelle Pathologie und Pharmakologie*, Vol. 46, p. 230.



preparations being generally preferred to their internal administration.

M. de Biehler also attributes to sodium cacodylate an arsenic-like action. In man it increases the hæmoglobin in the blood, though it diminishes the number of the red, and also of the white corpuscles. It also leads to an increase in weight, and an improvement in the general condition. It distinctly diminishes the oxidation power of the body, and it is therefore contra-indicated in any case in which there is any reduction in the power of oxidation. C. Chiappori came to the opposite conclusion, viz., that cacodylic acid caused an increase in the number of red blood corpuscles and a diminution in the hæmoglobin.

Dawes and Jackson found that about 6 to 10 p. c. of the sodium cacodylate applied subcutaneously is eliminated unchanged in the urine\*). On continued administration, or on using larger doses, it is said that the presence of inorganic compounds of arsenium may be readily detected in the urine. In these cases, as Chiappori has shown, arsenic is eliminated not only in the urine but also in the fæces. Sodium cacodylate, when administered by mouth, is said by Imbert and Badel to be in great part excreted with

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Biehler, Archives internationales de pharmacodynamie et de thérapie Vol. 17, p. 65, cf. Therapeutische Monatshefte 1907, p. 427.

Chiappori, Riforma medica 1901, No. 91.

Dawes-Jackson, Journal of the American Medical Association 1907, No 25, Semaine médicale 1907, p. 441.

\*) On the detection and estimation of cacodylic acid (in the urine) see:

Imbert and Astruc, Journal de pharmacie et de chimie 1899, II, p. 392.

Imbert and Badel, Comptes rendus de l'académie des sciences Vol. 129, p. 1244, Vol. 130, p. 581.

Barthe and Péry, Journal de pharmacie et de chimie 1901, I., p. 209.

Heffter, Schweizer Wochenschrift für Pharmazie Vol. 39, p. 139.

Vitali, Bollettino chimico farmaceutico 1901, Vol. 40, p. 657 and 1903, Vol. 42, p. 641.

Bougault, Journal de pharmacie et de chimie 1903, I., p. 97.

Ganassini, Bollettino chimico farmaceutico 1903, Vol. 42, p. 5.

Carlson, Zeitschrift für physiologische Chemie 1906, p. 410.

Bloemendal, Archiv der Pharmazie Vol. 246, p. 599.

Imbert-Badel, Münchener medizinische Wochenschrift 1900, p. 633.

the following passage of urine, while the remainder requires more than a month for its elimination.

The above mentioned results of the investigation of the physiological and pharmacological action of cacodylic acid show that many points still await definite elucidation. It appears to be desirable to test the accuracy of the statements of the authors mentioned by further trials with pure sodium cacodylate as is available at the present time, for it is by no means certain that all of them used reliable preparations. The process of manufacture has revealed the fact that more care and experience are necessary in the preparation of these pure substances than appeared on a superficial examination. It is therefore to be presumed that many of the authors referred to in the literature worked with a preparation that was not altogether reliable. Many of the contradictory statements can scarcely be explained in any other way. Further, the improvement in the process of manufacture of cacodylic acid has led to a considerable increase in its medicinal use. The definite proof of the therapeutic value of the cacodylates has been furnished by therapeutic experience\*).

The first to draw attention to the therapeutic use of cacodylic acid and thus to the use of organic compounds of arsenium was the Darmstadt physician Dr. Jochheim. It is clear that he relied on Bunsen's communication as to the non-toxic character of cacodylic acid, and tried it as a substitute for arsenic in chronic diseases of the skin. His results were very satisfactory.

With regard to this question, he says: "I regard cacodylic acid as the most important preparation of arsenic, and I introduced it into my practice two years ago. The usual compounds of arsenic, when carefully used and keeping the patient under careful observation, do no harm, and, further, when used in suitable cases they usually very quickly display a curative action. There exists, however, an

\*) In recognition of this fact, sodium cacodylate was accepted as an official preparation in the year 1907 in the *Pharmacopoea Helvetica*, 1908 in the *Pharmacopée française* and 1909 in the *Farmacopea ufficiale del regno d'Italia*.

Dr. Ph. Jochheim, *Über chronische Hautkrankheiten und ihre Behandlung in meiner Heilanstalt. Darmstadt 1864*. Published by Ollweiler. (See Péraldi, *Presse médicale* 1902, p. 22).

organic compound of arsenic, cacodylic acid, which contains arsenic and oxygen in the same proportions as arsenious acid, and which is remarkable on account of its possessing no poisonous properties on the animal organism. For this reason I determined to ascertain whether this non-poisonous arsenic compound might be used as a substitute for the usual preparations of arsenic." (Cacodylic acid was obtained by Jochheim from Obermedizinalrat Dr. Winckler in Darmstadt, who had prepared it himself). "So far I have used this preparation in 42 cases of chronic skin diseases. The cases included obstinate forms of psoriasis, impetigo, eczema and herpes. The result was entirely favourable, for by the use of this acid I was able to cure these diseases in a short time, usually without the aid of external remedies. In some cases of lupus, again, this preparation was of considerable service. At first I was very careful with the dosage of the remedy, for I had no other statements to rely upon except to the effect that it had no poisonous action, but no reports were known that proved that this preparation had been tried internally by anyone before me. I commenced with a dose of 0.015 gramme ( $\frac{1}{4}$  grain) of cacodylic acid 3 times a day, in alcoholic solution. I doubled the dose every 4 days, rising to 0.25 gramme (4 grains) for a dose. These doses I continued for 8 to 14 days, and then began to decrease the doses at the same rate as they had been increased. Since then it has been my custom to commence with a dose of 0.06 gramme (1 grain) and to increase this every 4 days by 0.06 gramme (1 grain) up to 0.3 gramme (5 grains), at which dose I remained for a time, and then began to reduce the doses at the same rate as I had increased them. I have never observed the occurrence of any harmful results from the use of this preparation. It was always well tolerated, even when other arsenic compounds were not borne. Consequently I consider myself justified in stating that it combines all the advantages of the arsenic preparations without possessing their disadvantages. I have tried the preparation in other diseases too, and have obtained excellent results with it in remittent fever, but particularly in chronic pulmonary tuberculosis on which I propose to report elsewhere\*). In any case the introduction of

\*) The author carried out this intention in a paper which appeared subsequently. See p. 18.



cacodylic acid appears to me to have been a distinct advance, and further trials in conditions of dyscrasia should meet with their reward.”

Jochheim's communications aroused little attention, and W. Th. Renz was the only one who adopted Jochheim's recommendation and used cacodylic acid in 5 cases, only two of which, however, were cases of skin disease. A single case of neuralgia was the only one in which the treatment resulted in a temporary amelioration of the pain. The author was discouraged from further continuing its use by observing that some time after commencing the treatment the patient's breath acquired a smell of garlic. If Renz, who was aware that cacodylic acid could be applied intravenously without harm, had used it in this way or by subcutaneous application, he would not have given up the use of the preparation so readily, and thus have prevented others from using it. It must be supposed that he used this method of administration of cacodylic acid without intermission, in which case the smell of garlic would have been particularly liable to occur. The single dose given by Renz amounted to 0.06 gramme (1 grain) and the total amount used to 4—5 grammes (60—75 grains). We may undoubtedly assume that the failure to obtain good results was due rather to the unsuitable method of administering it than to the remedy itself. It remained for the French physician Gautier 35 years later to definitely introduce cacodylic acid into therapeutics, and to establish its reputation; Danlos also contributed largely to this result, and his publications, in fact, are dated 2—3 years earlier than those of Gautier\*). The first communication of Danlos on the use of cacodylic acid was made on June 11, 1896, before the Dermatological Society of Paris; it dealt with the treatment of psoriasis. He stated that sodium cacodylate had given

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Renz, *Deutsches Archiv für klinische Medizin* 1865, p. 235.

Gautier, *Bulletin de l'Académie de médecine* 1899, p. 604. — *Semaine médicale* 1899, p. 364. — *Presse médicale* 1899, p. 215, 1900, p. 94, 1901 p. 3 and 13, 1910 p. 848.

Danlos, *Semaine médicale* 1899, p. 213. — *Revue de thérapeutique* 1899, p. 464. — *Presse médicale* 1897, p. CCXXIII. — *Therapeutische Wochenschrift* 1896, p. 601 and 1897, p. 561.

\*) Danlos, *Société médicale des hôpitaux*, Nov. 25, 1910.

very good results on the internal administration of 0.25 gramme (4 grains) daily, or following the subcutaneous injection of doses of 0.1 gramme ( $1\frac{1}{2}$  grains) daily. About a year later the author showed the Society a case of obstinate psoriasis cured by sodium cacodylate. In the treatment of this case he had used the following formula:

Rp. Sod. cacodyl.	2.5 (38 grains)
Rum.	
Syr. aurant. aa.	20.0 ( $\frac{2}{3}$ oz)
Ol. menth. pip. min. II.	
Aq. destill.	60.0 (2 oz)

The patient was able to take 6 teaspoonfuls of this mixture daily without difficulty, and improvement set in very quickly. The only disadvantage accompanying this treatment, in addition to the smell of garlic towards the end of the third week of treatment, was some degree of intolerance on the part of the stomach. Danlos reported a case of pseudo-leukæmia in which he had given ten injections of 0.15 gramme ( $2\frac{1}{3}$  grains) each of sodium cacodylate within three weeks. He found that the injections were well borne, while the weight of the patient, which had diminished considerably before treatment with cacodylic acid, began to increase under its influence. The glands, however, had not diminished in size under its use. Other cases were published by Danlos in the year 1899 of the treatment of psoriasis, acne, lichen planus, lupus erythematosus, cutaneous tuberculosis, dermatitis herpetiformis, adenitis tuberculosa, sarcoma of the skin, sarcoma of the lymphatic glands and mycosis fungoides.

Gautier first suggested cacodyle treatment in the year 1899. He pointed out that cacodylic acid, being an organic compound of arsenium, did not show the unpleasant secondary effects of Fowler's solution. He recommended the subcutaneous use of the remedy to obviate the possibility of secondary action on the stomach, and to prevent the smell of garlic which followed its internal administration. He found cacodylic acid to aid nutrition, to increase the activity of the nutrition, to increase the activity of the blood corpuscles, and to favour hæmatosis. He therefore regarded it as the best form of treatment in pulmonary tuberculosis, anæmia,

malaria and constitutional affections. In tuberculosis he recommended daily injections of 0.05 gramme ( $\frac{3}{4}$  grain) of sodium cacodylate, to be continued for 8 days and then discontinued for a further period of 8 days. For these injections he gave the following prescription:

Rp. Sodii. cacodyl.           6.4 (96 grains)  
Aq. destill.               100.0 ( $3\frac{1}{3}$  oz)  
Alcohol carbolisati gtt. X.

This solution is easy to sterilise; 1 c. c. (17 min.) corresponds to 0.05 gramme ( $\frac{3}{4}$  grain) of cacodylic acid. A similar injection fluid recommended by the author is as follows: 5 grammes of cacodylic acid are dissolved in 80 c. c. of water. This solution is neutralised as accurately as possible with sodium carbonate. 0.08 gramme of cocaine hydrochloride and 5 drops of creosote dissolved in 8 grammes of alcohol are added. This mixture is made up to 100 c. c. with water. If tuberculous patients show a tendency to hæmorrhage, congestion and hæmoptysis, or if in women menstruation sets in, Gautier advises that the treatment be discontinued. He also prescribes potassium bromide and iodide, and a diet rich in phosphates and iron. Other indications mentioned by Gautier in the course of his communications are general debility, cachexia, neurasthenia, scrofula and syphilis, and in these conditions sodium cacodylate is said to have given good results.

Coincident with Gautier and Danlos, the therapeutic value of cacodylic acid was studied by Prokhoroff who sums up his conclusions as follows:

Cacodylic acid is to be included among those compounds of arsenium which can be borne by the animal organism in very large doses. It is therefore to be regarded as non-toxic in contrast to the ordinary preparations of arsenium. No matter whether applied internally or subcutaneously cacodylic acid has a tonic action which shows itself by an improvement in the general condition, increased appetite and a gain in weight. The tonic action is particularly evident at the commencement of treatment, and diminishes somewhat after a time. The gain in weight, however, is in very many cases a permanent one. Even in large doses cacodylic acid causes no intestinal disturbance. Its decomposition in



the organism takes place very rapidly, and the elimination of its final products takes place principally by the lungs and the kidneys.

Rénaut, who had obtained successful results in various diseases by the rectal use of Fowler's solution, although he had not been able to avoid the irritant effects of this preparation, turned his attention to cacodylic acid. In his experience the intestinal mucous membrane is not irritated by sodium cacodylate solution. It may therefore be introduced as often as necessary. For this purpose he gives two solutions differing in concentration:

1. A weak solution, consisting of 0.25 gramme (4 grains) of sodium cacodylate and 200 grammes ( $6\frac{2}{3}$  oz) of water;
2. A strong solution, 0.4:100.

One or other of these solutions is administered per rectum, two injections of 5 c. c. being made daily for the first 6 days, and three daily for the following 6 days; another series of injections being commenced after an interval of 5 days. Various dyscrasias, such as tuberculosis, Graves' disease, diabetes and cancer of the stomach are the indications for the use of sodium cacodylate given by Renaut. In tuberculosis that is not too far advanced, and in the so-called pre-tuberculous stages, this treatment is said to give very good results, checking the development of the tubercle bacilli, when combined with suitable diet, rest and open-air treatment. In diabetes sodium cacodylate may be combined with antipyrin. In gastric cancer, the rectal treatment results in an improvement in the general condition and a gain in strength. In leukæmia, again, Renaut obtained rapid improvement by this treatment. The action of cacodylic acid is supposed by the author to be due to a gradual accumulation of the arsenium in the histological elements of the nervous system, forming arsen-lecithins, while it spares the albumin.

The introduction of the cacodylates in therapeutics was furthered by the publications of H. Gijsselmans, Podar-

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Rénaut, Bulletin médical 1899, No. 45. — Münchener medizinische Wochenschrift 1899, p. 947.

Gijsselmans, Dissertation Freiburg 1898. — Wiener klinische Wochenschrift 1899, No. 14.

nowski, G. Verotti and H. Rille. These authors obtained good results by the subcutaneous application of sodium cacodylate in skin diseases, particularly in psoriasis and lichen ruber planus. Gijsselmans used it by injection into the glutei with good results.

We shall now examine the results obtained since the introduction of the cacodylates in therapeutics by various authors and practitioners, and the indications for the use of the cacodylates.

### Skin diseases.

In addition to the authors already named, E. Saalfeld, Gaucher, L. Wickham, G. Löwenbach and B. Klinger have made contributions to the treatment of skin diseases. Saalfeld used pills of sodium cacodylate in his trials. His usual dose was 0.05 gramme ( $\frac{3}{4}$  grain) for a dose, and 0.1 gramme ( $1\frac{1}{2}$  grains) daily. Subcutaneously he used 1 c.c. of a 5 p.c. aqueous solution of sodium cacodylate, put up in sterile ampoules. The contents of one ampoule were injected every day. Per rectum he used injections of 0.05 gramme ( $\frac{3}{4}$  grain) for a dose, or suppositories containing the same amount. He treated 50 patients suffering from various skin affections such as psoriasis, severe itching, lichen ruber planus, herpes iris, etc. In particular he ascertained that sodium cacodylate had the advantage over the usual inorganic preparations of arsenium of being better tolerated, for his patients took the remedy well in nearly every case, and this applied even to patients in whom Fowler's solution produced gastric disturbances. With regard to the smell of garlic mentioned by several authors as following the internal administration of sodium cacodylate, this smell was observed by Saalfeld in only a third of the patients he treated. He considers that this secondary action occurs principally in anæmic persons whose gastric and in-

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Podanowski, Bolnitsch. Gaceta Botkina 1899, No. 25.

Verotti, Arte medica 1900, No. 47.

Rille, Archiv für Dermatologie und Syphilis 1898, p. 5 and 42.

Saalfeld, Therapeutische Monatshefte 1901, p. 285.

Gaucher, Semaine médicale 1901, p. 197.

Wickham, Semaine médicale 1901, p. 197.

Löwenbach, Wiener klinische Wochenschrift 1903, No. 9. — Therapeutische Monatshefte 1903, p. 489.

Klinger, Wiener medizinische Wochenschrift 1904, No. 5.

testinal functions are not normal. He never noticed a smell of garlic to follow the subcutaneous and rectal use of the remedy. His patients did not complain of any of the unpleasant secondary effects that are apt to occur with the customary preparations of arsenium, such as diarrhoea, dry throat and aching eyes. From a therapeutic point of view his results were very favourable. The author places special emphasis on the fact that sodium cacodylate provides us with a preparation of arsenium which may be applied subcutaneously without fear of producing local irritant effects. Moreover, he considers this method of administration to be far more effective than the internal method.

Gaucher and Wickham report their results in the treatment of mycosis fungoides. Gaucher was able to cure a case of this kind in a few weeks by means of cacodylic acid. The disease returned later, however, with increased severity. Wickham, on the contrary, obtained very encouraging results in a case of mycosis. In a comparatively short time he obtained a cure by the injection of gradually increasing doses of cacodylic acid, repeated at intervals. If renewed itching of the skin occurred from time to time he was always able to relieve it by a few injections. Gastou, Leredde and Brocq also speak favourably of this form of treatment.

Klinger treated a patient suffering from diffuse psoriasis who had failed to receive any benefit from baths, soap applications, tar, chrysarobin and white mercury ointment after lengthy trials. In this case the internal administration of arsenic had likewise proved ineffective. He gave a daily injection of 0.05 gramme ( $\frac{3}{4}$  grain) of sodium cacodylate for 10 days, followed by a pause of 10 days. The troublesome itching subsided after the first series of injections. In the course of the subsequent treatment no new efflorescences sprang up, while the scaling spots grew paler and eventually disappeared. Six series of injections were required in all to produce a complete cure, so that altogether 3 grammes (45 grains) of sodium cacodylate were used. In addition to the cure of the skin affection there was a gain in weight amounting to 8 kilogrammes ( $17\frac{1}{2}$  lb.). No secondary effects, such as abscesses and inflammation of the skin, were produced by the injections. In psoriasis complicated



with syphilis, sodium cacodylate also gives good results, as is apparent from the communications of Löwenbach. (See below.)

### Syphilis.

The value of cacodylic acid and of sodium cacodylate in syphilis has been described by Gautier. He took it for granted that arsenium treatment had no specific action on this disease, its valuable therapeutic effect being due merely to its pronounced beneficial influence on the general condition. Cacodylic acid was therefore used in syphilis principally in combination with iodine and mercury. (See *hydrargyri cacodylas*.) Of recent communications on the treatment of syphilis that of M. Oppenheim is of interest. This author prefers sodium cacodylate to the more recent preparations of arsenium, such as atoxyl and amino-phenyl-arsinic acid, because it is less toxic. He prescribed it in a 20 to 25 p.c. solution, of which he injected doses of 1 c.c. (17 min.) subcutaneously, a procedure which he considers absolutely free from danger. As regards the results of his treatment, he comes to the following conclusions: The ulcers in malignant syphilis become clean after the 5<sup>th</sup> injection, and begin to heal. After the 20<sup>th</sup> injection most of the ulcers had healed. The ulcers cicatrized from the centre, but after the 15<sup>th</sup> injection no further improvement occurred, and it was found necessary to use salicylate of mercury. Gummata of the leg healed after 15 injections. Sodium cacodylate was also found to be useful for preventive treatment.

In syphilis a thorough trial of sodium cacodylate is specially to be recommended, for the most recent communications of J. B. Murphy show that it produces the same results as those obtained with the newer preparations of arsenium. Sodium cacodylate has the advantage of being readily soluble in water, very stable, and may be sterilised without fear of decomposition, while it is so cheap that it is available in all cases. A point which deserves special prominence is the fact that after 10 years' fairly extensive use in therapeutics no dangerous symptoms of poisoning have been observed. No single case of blindness after the injection

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Oppenheim, *Klinisch-therapeutische Wochenschrift* 1907, p. 1170.

Murphy, *Journal of the American Medical Association* 1910, Vol. 55, No. 13, p. 1113.

of sodium cacodylate has come to my knowledge. It will therefore be interesting to await the results of Murphy's comparative investigations of sodium cacodylate and Ehrlich's remedy "606".

### Carcinoma and Sarcoma.

On the treatment of carcinoma with subcutaneous injections of sodium cacodylate there are two communications by E. Payne and Launois. Both authors have seen good results in inoperable carcinoma from treatment with cacodylic acid. Payne believes that in his cases he undoubtedly obtained a prolongation of life. Petrini reports that he has cured a case of sarcoma of the pharynx by injections of sodium cacodylate. Mendel, however, had to report a complete failure in a case of carcinoma of the mamma which he treated with intravenous injections. Renault, in a case of epithelioma of the tongue, gave 1—5 pills daily, each containing 0.05 gramme ( $\frac{3}{4}$  grain) of sodium cacodylate. He states that he obtained a very satisfactory result in one case in particular.

### Malaria.

In malaria and malarial cachexia, sodium cacodylate has given good results in the hands of H. Billet, A. Jalaguier and Barth and W. Ewart, both internally, and on rectal and subcutaneous use. Billet considers the preparation to be particularly indicated in cases of malaria in which full doses of quinine have given rise to the injurious action on the blood which follows quinine treatment. This injury is said to be greatly modified by the cacodylate.

### Trypanosomiasis.

Considering the great interest that has been shown in the new preparations of arsenium, it is strange that a

Payne, *Lancet* May 25, 1901.

Launois, *Deutsche medizinische Wochenschrift* 1901, p. 95 (Supplement). — *Lyon médical* January 27, 1901.

Petrini, *Presse médicale* 1900, p. 65.

Mendel, *Therapeutische Monatshefte* 1902, p. 182.

Renault, *Presse médicale* 1900, p. 114.

Billet, *Revue de thérapeutique* 1900, p. 626. — *Presse médicale* 1902, p. 154.

Jalaguier-Barth, *Presse médicale* 1901, p. 105.

Ewart, *Münchener medizinische Wochenschrift* 1901, p. 120.

thorough trial of the cacodylates has not yet been made in the treatment of sleeping sickness. As far as I know the only pharmacological publication up to the present is that of Massaglia, who demonstrated by animal experiment that sodium cacodylate had a specific action on the trypanosomes. Gautier found that a subcutaneous dose of 0.5 gramme ( $7\frac{1}{2}$  grains) of sodium cacodylate was tolerated without setting up any secondary effects, and it would therefore seem to follow that the preparation should be of great service in dealing with trypanosomes. A communication of Pflughöft shows that in a case of kala-azar sodium cacodylate gave good results for months. The success of the treatment, however, was limited to the first years of the disease, after which the remedy failed to act. There is no doubt that in this case the parasites which caused the disease had gradually accustomed themselves to the preparation, and had become immune to cacodyle. The same phenomenon has of late years been observed with other arsenium preparations, such as atoxyl and arsacetin.

#### Leprosy.

Raynaud has given subcutaneous doses of 0.05—0.1 gramme ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains) of sodium cacodylate daily in leprosy, and has obtained remarkable results. The effect of the treatment was not only to improve the general condition and to produce an increase in weight, but it also effected a considerable improvement in the local condition coupled with the healing of the leprous swellings. In the treatment of this disease it is necessary to give the drug for months or years. It is not advisable to give the injections continuously, but in series with suitable intervals.

#### Pott's Disease.

In a case of angular kyphosis Bayeux had applied a plaster corset without appreciable success. The patient was a girl aged 11. The disease was advancing rapidly and the patient was anæmic, febrile, and suffered from loss of appetite

Massaglia, *Riforma medica* 1907, No. 7.

Gautier, *Münchener medizinische Wochenschrift* 1901, p. 1365.

Pflughöft, *Münchener medizinische Wochenschrift* 1910, p. 1395.

Raynaud, *Bulletin médical de l'Algérie* 1901, November.

Bayeux, *Annales de médecine et chirurgie infant.* 1900, No. 15.



and consequent extreme wasting. The author began with doses of 0.03 gramme ( $\frac{1}{2}$  grain) of sodium cacodylate daily in the form of pills given by mouth, coupled with complete rest in bed. He then proceeded to the subcutaneous administration of the remedy, giving 0.05 gramme ( $\frac{3}{4}$  grain) every second day. The fever and the general condition improved in the course of a few days, and after a month's treatment the disease was brought to a standstill. It was not to be expected, of course, that the curvature of the spine would right itself, but in other respects the results of the cacodylic acid treatment were so favourable that the author recommends further trials. Even in tuberculous osteitis and osteo-arthritis in children, and in coxalgia, the author believes that satisfactory results should be obtained from the use of the cacodylates. This view is fully justified, for tuberculosis is an indication in which cacodylic acid treatment was used first of all with the greatest expectations.

#### Tuberculosis.

Jochheim already drew attention to the use of cacodylic acid in tuberculosis. In his publication on pulmonary tuberculosis\*) he writes as follows: "I used cacodylic acid dissolved in dilute alcohol, and gave 0.015 gramme to 0.03 gramme ( $\frac{1}{4}$ — $\frac{1}{2}$  grain) 3 times a day. I then increased the dose every 3 to 4 days by 0.015 gramme ( $\frac{1}{4}$  grain) until I had reached doses of 0.25—0.3 gramme (4—5 grains). I then began to diminish the dose at the same rate as I had increased it. I never observed any harmful secondary action to follow the use of this preparation. It was always well borne, even when other compounds of arsenium were not tolerated. In the large number of cases in which I have used cacodylic acid I can recall only two in which doses of 0.25—0.3 gramme (4—5 grains) were given for some time, and in which loss of appetite, thirst, vomiting and diarrhoea appeared, these symptoms subsided again without producing any harmful by-effects as soon as the remedy was left off, and then given again later in smaller doses. The most successful results with this preparation, in addition to the treatment of chronic skin diseases, were observed in chronic pulmonary

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\*) Ph. Jochheim, "Die chronische Lungenschwindsucht ist heilbar". Darmstadt, Published by W. Ollweiler. 1865.

tuberculosis. When used consistently for several weeks in this affection it invariably leads to a feeling of warmth in the stomach, an improvement in the appetite and an increase in the urinary and intestinal secretion. The general condition of the patient shows a well-marked change for the better, his cachectic appearance vanishes, he acquires a certain freshness, gains in weight, his veins become injected and his blood darker in colour. At the same time expectoration is facilitated, the cough becomes less troublesome, the breathing easier and deeper, while the physical examination convinces us before long that the tuberculous process is subsiding. I have succeeded, merely by the administration of cacodylic acid, in producing a complete cure of chronic pulmonary phthisis in the first stage in several cases, and in other more advanced cases I have at any rate produced so much benefit as to improve the prospect of life by several years. Most likely cacodylic acid displays its beneficial curative action in this disease by reducing the irritant condition of the lungs by causing hyperæmia of the abdominal organs, all the symptoms described above following its use point to this conclusion. Its action would thus be due to its imparting to the blood a venous character, inimical to tubercle bacilli." Gautier and Danlos have from the first given tuberculosis as one of the principal indications for the use of cacodylic acid. Other very favourable reports on this subject have been published by Letulle, Mouisset, F. Widal, P. Merklen, Dalché, Rocaz, Kock, Allard, Levrat, Variot, Evoli, Skuteki, Collet, P.

Letulle, *Presse médicale* 1900, No. 34.

Mouisset, *Bulletin médical* 1900, No. 89, p. 1227.

Widal, Merklen, Dalché, *Presse médicale* 1900, No. 20. — *Thérapeutique Monatshefte* 1900, p. 497.

Rocaz, *Semaine médicale* 1900, No. 45. — *Bulletin médical* 1900, No. 97.

Kock, *Nordisches medizinisches Archiv* 1902, II. No. 2, p. 74.

Allard, *Thérapie der Gegenwart* 1902, p. 494.

Levrat, *Revue internationale de médecine et de chirurgie* 1905, p. 96.

Variot, *Journal des praticiens* 1905, No. 49.

Evoli, Paper read at the 11<sup>th</sup> Italian Congress for internal medicine, October 1901.

Skuteki, *Gazzetta degli ospedali e delle cliniche* 1901, No. 99.

Collet, *Dissertation Paris* 1902.

Gallois, Burlureaux, A. Latarjet, W. Ewart, Dalché, Mendel, Meillant and A. Billet.

All these authors have obtained very good results with cacodylic acid treatment, though Allard believes the action to be due to suggestion. We are bound to admit that in the case of the cacodylates we are not dealing with a specific treatment. The reports of the above-named authors show, however, that the cacodylates form a very valuable auxiliary remedy in the treatment of pulmonary tuberculosis. Particularly in the first stages of the disease they are of excellent service if they are given in good time. Improvement is frequently produced, the cough diminishing, the night sweats leaving off, the fever abating and the general strength showing a definite increase. In advanced cases of phthisis, however, one should not expect much good from its use. For internal administration Dalché considers the pill to be the most suitable form. He gave one pill (containing 0.025 gramme [ $\frac{2}{5}$  grain] of sodium cacodylate) every day for 4 days, and then two pills a day for about 30 days. Meillant prescribed cacodylic acid in the following form:

Rp. Sod. cacodyl.	0.02 gramme	( $\frac{1}{3}$ grain)
Thiocol	0.5—1.0	„ ( $7\frac{1}{2}$ —15 grains)
Calc. glycerophosph.	0.5	„ ( $7\frac{1}{2}$ grains)
Nuc. vomic. pulv.	0.01	„ ( $\frac{1}{6}$ grain)
M. Ft. pulv. Mitte XX.		

2 to 3 of these powders are given daily for 12 days, after which thiocol (potassium-guaiacol-sulphonate) is given by itself in suitable doses for 8 days. Afterwards the above prescription is again used alternately with thiocol at equal intervals.

In children Rocaz gave sodium cacodylate in an aqueous solution after meals. Children of 2 to 14 years were given 0.01—0.04 gramme ( $\frac{1}{6}$ — $\frac{2}{3}$  grain) a day divided into two doses. He states that children of 3 to 4 years may be

Gallois, Bulletin de thérapeutique 1901, p. 567.

Burlureaux, Bulletin de thérapeutique 1901, p. 524.

Latarjet, Lyon médical 1900, p. 370.

Ewart, Münchener medizinische Wochenschrift 1901, p. 120.

Dalché, Presse médicale 1900, p. 72.

Mendel, Therapeutische Monatshefte 1902, p. 178.

Meillant, Concours médical 1906, No. 10.

Billet, Presse médicale 1902, p. 573.



given 0.01 gramme ( $\frac{1}{6}$  grain) daily, children of 6 to 10 years 0.02—0.03 gramme ( $\frac{1}{3}$ — $\frac{1}{2}$  grain) and of 10 to 15 years 0.03—0.04 gramme ( $\frac{1}{2}$ — $\frac{2}{3}$  grain).

If the expired air acquires a strong smell of garlic after the internal use of sodium cacodylate, the treatment is interrupted, and in all cases it is advisable to intermit the administration from time to time, or to go on with subcutaneous doses. Subcutaneous exhibition is probably the best mode of administration in any case. The average dose is 0.05 gramme ( $\frac{3}{4}$  grain). The various authors suggest doses varying between 0.02—0.1 gramme ( $\frac{1}{3}$ — $\frac{1}{2}$  grains). Levrat obtained better results by injecting doses of 0.3 gramme (5 grains) at intervals of several days, e. g., 4 to 8 days, than by giving small doses every day. This observation is of importance to the practitioner for it obviates the necessity of frequently visiting the patient. A dose of 0.15 gramme ( $\frac{2}{3}$  grain) is given to ascertain whether the particular patient will stand large doses. Levrat reports that he has treated more than 200 tuberculous patients with sodium cacodylate in this manner in the last 18 months, and obtained very satisfactory results. The communications of Bayeux show that there is no need for undue caution in the dosage of the cacodylates. This author has been led by his favourable results with cacodylate treatment to place particular confidence in this drug. He considers that the doses that have hitherto been used in tuberculosis were too small for the achievement of really good results. As he has performed 12,000 injections and never observed any harm, he uses, even in children, subcutaneous doses of 0.2 to 0.6 gramme (3—9 grains) which are repeated as often as 3 times a week. In one hopeless case of tuberculosis of the tibio-tarsal joint he injected as much as 2 grammes (30 grains) for a dose with complete success. The smallest dose for surgical cases is given by him as 0.3 gramme (5 grains) (3 times a week) and for medical cases 0.1 to 0.2 gramme ( $\frac{1}{2}$ —3 grains). In this way he obtained good results in pulmonary tuberculosis in the first and second stages. In using these large doses, however, we must not use concentrated solutions, for these are usually painful. Bertherand also favours solutions of not more than 5 p. c.

strength, though Danlos has used solutions of 25 p. c. without causing secondary effects.

A point of special importance is that Levrat and Bayeux have observed no secondary effects even with these high doses. It is true they always tested the sensibility of their patients for cacodylates; they allowed suitable intervals during the treatment, and were particularly careful in cases presenting kidney trouble. Sodium cacodylate may also be used intravenously, and L. Anelli has drawn attention to this mode of exhibition. He gives intravenous doses of 0.05 gramme in 1 c. c. of water. Mendel also used a 5 p. c. aqueous solution of which he injected 1—3 c. c. In his experience the intravenous method is in every respect superior to all other methods of application. In apical catarrh with infiltration of one or both lobes of the lung and occasional attacks of fever (rising to 35.8° C.), Mendel observed an improvement in the general condition after a few intravenous injections, while the appetite and the appearance were improved and there was a gain in weight. At the same time the cough and the phlegm left off. After 2 to 3 months' treatment there appeared in some of the patients in place of the crackling sounds, clear vesicular breathing, so that they could be regarded as cured. In other cases there was a subjective and objective improvement such as the author seldom observed with any other method of treatment. An excellent result was obtained by intravenous treatment in a case of tuberculous testes in which suppurating fistulæ and abscesses had appeared after operation, and had reduced the patient's strength to the uttermost. With the introduction of cacodylate treatment a complete transformation in the course of the illness soon set in. The fistulæ closed rapidly, the urine became clear and was passed without pain, the troublesome strangury left off, and after five weeks the patient had gained 15 lbs in weight. Mendel also tried a combination of sodium cacodylate with hetol, but his results were no better than with the cacodylate alone.

Burlureaux prefers the intramuscular application of sodium cacodylate in doses of 0.05—0.1 gramme ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains), administered as a 5 p. c. aqueous solution, and although

Anelli, *Riforma medica* 1901, No. 167. — *Semaine médicale* 1901, p. 248.

he gave these injections every two days for 15 months in some cases, he never observed even the slightest symptom of intolerance.

Schmitt and Traverse report on the advantages of the use of cacodylates in tuberculous peritonitis. In one desperate case they used the following method of treatment: Every morning the patient was given an injection of 0.05 gramme ( $\frac{3}{4}$  grain) of sodium cacodylate and an enema consisting of 5 grammes (70 min.) of carbon bisulphide in 500 grammes (17 oz) of water, coupled with high feeding. 73 days after the beginning of the cacodylic treatment the patient might be regarded as cured. He was given cacodylate of iron for a time as he stood it very well.

#### Asthma and Bronchitis.

A. Martinet gives constitutional asthma as another indication for the use of cacodylic acid. In this case, however, treatment by injections is the only method that is likely to prove successful. Gallois, who endeavoured to cure asthma and emphysema by the internal administration of the drug, did not obtain the desired results. In chronic bronchitis in elderly people, however, where asthmatic attacks were apt to occur, this treatment was found very useful. His prescription is as follows:

Rp. Sod. cacodyl.	2.0 grammes (30 grains)
Spirit. Sacchari	
Syrup.	20.0 „ ( $\frac{2}{3}$ oz)
Aq. destill.	60.0 „ (2 oz)
Spirit. menth. pip. min. II	

Of this mixture one teaspoonful is given after each meal. After 8 days it is discontinued for 8 days, and is then resumed, this intermittent treatment being continued.

#### Chlorosis, Anæmia and Leukæmia.

These diseases were almost the first indications given for cacodylic treatment, for in them the favourable effects of the use of arsenium have been long known. Thus Jochheim, Danlos and Gautier report that cacodylic acid is evi-

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Schmitt-Traverse, Société de thérapeutique, Séance du 17 avril 1901. — Journal de pharmacie et de chimie 1901, I, p. 546.

Martinet, Presse médicale 1901, p. 105.

Gallois, Münchener medizinische Wochenschrift 1901, p. 1988.



dently destined to play an important part in the treatment of diseases of metabolism and of the blood. This would appear to refer only to the Latin races and the reason for this may be sought in the fact that impure commercial products have produced secondary effects which have brought the cacodylates into disrepute, and this appears to be the case in Germany. At any rate the cacodylates should be given greater consideration in the more severe cases in which their subcutaneous administration is less fraught with danger. But even in less severe cases, in which arsenium treatment is indicated, a trial with the cacodylates of sodium and iron given internally would frequently meet with its reward. Should a smell of garlic occur it is easy to change the medicine.

A. Bormans recommends sodium cacodylate in anæmia and chlorosis, particularly if iron preparations are not tolerated. Renaut obtained good results by the use of sodium cacodylate in a case of leukæmia, and Ewart is certain that successful results will follow its employment in pernicious anæmia. Otherwise cacodylate of iron has been generally used in these diseases (see the article on page 29).

Very favourable reports on the cacodylate treatment of anæmia and chlorosis have been made by Mendel. In slight cases the treatment took four weeks. He began by injecting (subcutaneously or intravenously) 0.05 gramme ( $\frac{3}{4}$  grain) every two days, and increased the dose gradually to 0.1 gramme ( $1\frac{1}{2}$  grains). In severe cases he increased the dose to 0.2 gramme (3 grains) and gave an injection every day. After three weeks' treatment he made a pause of 8 days, and then recommenced the treatment. The author only gave sodium cacodylate internally in exceptional cases, in the form of pills or mixtures. With this treatment Mendel observed a decided change for the better after a short time: the feeling of weakness, headache, palpitation and weariness were relieved, the appetite was improved, the weight increased and the mucous membranes assumed a better colour. In short, the result was considerably better than that obtainable on an average with iron treatment.

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Bormans, *Gazzetta degli ospedali e delle cliniche* 1900, No. 39.

Renaut, *Münchener medizinische Wochenschrift* 1899, p. 947.

Ewart, *l. c.*

### Nervous and Mental Diseases.

The cacodylates have been used by Gautier in the treatment of various mental diseases. Paulet is of opinion that acute functional disturbances, such as melancholia and depression with malnutrition, are best suited for this form of treatment. Garand, Chiappori, Ewart, Martinet and Launois have obtained some very good results in chorea. Subcutaneous exhibition would appear to be the most suitable method of administration, and is particularly recommended by Paulet. Some of these authors have also treated neurasthenia successfully with the use of the cacodylates. Mendel has reported some cases of nervous disturbance in which sodium cacodylate gave good results. Thus in an obstinate case of sciatica he injected 0.075 gramme ( $1\frac{1}{6}$  grain) of the preparation straight into the nerve. After 14 days' treatment, using 8 injections, the disease could be regarded as cured, although it had resisted treatment with injections and oral administration of aspirin, potassium iodide and light baths for 5 weeks. The author was also able to effect a rapid cure in a case of pressure paralysis of the radial nerve by injections into the affected arm. The hysterical weakness of the muscles of both legs in the case of a young girl was practically cured in a comparatively short time by 15 injections. In migraine Mendel regards the intravenous injection of sodium cacodylate as a specific form of treatment, leading to a rapid and permanent cure. One of the most recent communications confirms the value of sodium cacodylate in neurasthenia. H. Willige found the preparation to be of good service in functional nervous diseases, particularly in neurasthenia due to anæmia. He used a solution of 1.5 grammes of sodium cacodylate, 0.1 gramme of cocaine hydrochloride and 3 drops of liquid carbolic acid in 50 c.c. of water. He directs that an injection

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Paulet, Thèse de Paris 1901. — British Medical Journal 1901, No. 2121, Epit. p. 32.

Garand, Semaine médicale 1900, p. 110.

Chiappori, Riforma medica 1901, No. 91.

Ewart, Münchener medizinische Wochenschrift 1901, p. 120.

Martinet, Presse médicale 1901, p. 105.

Launois, British Medical Journal 1901, I. Epit. p. 215. — Presse médicale 1901, p. 89 and 140.

Mendel, Therapeutische Monatshefte 1902, p. 182.

Willige, Münchener medizinische Wochenschrift 1910, p. 621.

be first given amounting to 4 divisions of a Pravaz syringe, increasing the injection daily by one division up to 20, and remaining at this amount for 14 days, after which the initial dose is resumed. The same treatment may then be tried with 5 p.c. solutions of cacodylate. Although the author has not observed the occurrence of harmful effects from the use of sodium cacodylate, he believes that the preparation is not to be regarded as an indifferent substance.

### Struma and Graves' Disease.

After Gautier and Ewart had recommended the use of sodium cacodylate in Graves' disease, Mendel made some trials in this direction. One patient was unaffected by cacodylate treatment. This was a woman of 38 suffering from severe cardiac disturbance, exophthalmos, but no enlargement of the thyroid gland was present. In another case, however, this treatment gave very satisfactory results, in a woman with slight exophthalmos, a moderately enlarged thyroid, palpitation, pulse-rate 180, tremors, sweating, excitation and attacks of migraine coupled with vomiting. The author prescribed an intravenous injection of 0.05—0.1 gramme ( $\frac{3}{4}$  to  $1\frac{1}{2}$  grains) of sodium cacodylate every two days, with the result that the attacks of migraine did not return, the struma disappeared completely after 4 weeks, and the pulse-rate fell to 100. In a case of thyroid disease the author tried intraparenchymatous injections into the tissue of the thyroid. He gave 3 series of injections with suitable intervals, and the treatment resulted in effecting a considerable diminution in the size of the goitre.

### Phosphaturia.

In certain forms of phosphaturia Lefebure obtained good results. It is said that equally good results are obtained whether sodium cacodylate be given internally or subcutaneously. The author gave doses of 0.03—0.1 gramme ( $\frac{1}{2}$  to  $1\frac{1}{2}$  grains) a day, and obtained a marked effect. The internal administration may be continued until the phosphaturia has disappeared, it is then advisable to discontinue the treatment. It is best to give the remedy for 15 days and then leave it off for 15 days before recommencing with



another fortnight's treatment. The result is stated by the author to be most certain in diabetic and rachitic phosphaturia, while it fails partially or entirely in pre-tuberculous, tuberculous, nervous and dyspeptic phosphaturia. Further, sodium cacodylate is said by Gautier and Mendel to display its tonic properties and good effect in

**Diabetes mellitus.** Gautier believes that the cacodylate occasionally has the same action as displayed by organotherapy as inaugurated by Brown-Séquard. This agrees with Mendel's results inasmuch as this author obtained with sodium cacodylate not only an improvement in the general condition, but found that it stimulated the sexual activities.

### Eye Affections.

In keratitis bullosa and other eye affections in which arsenium medication is indicated, Galezowski has observed excellent results to follow the use of sodium cacodylate. In these cases he combines its internal or subcutaneous use with external application in the form of eye drops or collyria. This author uses the following prescription:

Rp. Sod. cacodyl.	0.12 gramme (2 grains)
Cocain. hydrochlor.	0.25 gramme (4 grains)
Paraffin liquid.	15.0 grammes ( $1\frac{1}{2}$ oz)

M. Sig.: A few drops to be instilled into the eye two to three times a day.

The excellent results obtained by Bonsignorio from the external use of sodium cacodylate in corneal ulcer and ulcerous blepharitis should encourage further trials. In superficial and deep ulcers the results are excellent, the sores healing rapidly from their edges and leaving comparatively slight corneal opacity. Either a 3 p. c. aqueous solution of sodium cacodylate is used, 5 drops being instilled every morning for 15 days, or a 2 to 3 p. c. ointment is applied, a little being used every day for 8 days, and then every other day.

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Gautier, Bulletin médical 1899, No. 46.

Mendel, Therapeutische Monatshefte 1902, p. 181.

Galezowski, Recueil d'ophtalmologie 1902, March. — Merck's Archives 1905, p. 173.

Bonsignorio, Presse médicale 1908, p. 246.

In veterinary practice too the use of sodium cacodylate has recently been introduced\*), as is apparent from the communications of Marchal, Brunet and Lanceleur. Marchal successfully treated syphilis in horses with subcutaneous injections of 1 gramme (15 grains) dissolved in 5 grammes (85 min.) of water, given daily. Brunet and Lanceleur found that the preparation gave excellent results in weakness and malnutrition in dogs and horses. The daily dose for subcutaneous use is 0.05 gramme ( $\frac{3}{4}$  grain) in the case of a fox terrier, and 0.5 to 0.75 gramme ( $7\frac{1}{2}$ —11 grains) for a horse.

With regard to the possible injurious secondary effects of cacodylate treatment, I have already pointed out several times in the preceding pages that its internal administration is frequently followed by the occurrence of a smell resembling garlic in the breath (and also in the sweat). This fact was observed at the time of the introduction of the cacodylates by Gautier, Balzer and Griffon, and for this reason the subcutaneous method of application was recommended. In the early days of this form of medication, however, other secondary effects were observed resembling those produced by the use of arsenic, although less severe. Thus Balzer and Griffon mention two cases in which doses of 0.5 gramme ( $7\frac{1}{2}$  grains) per day produced fever, anorexia, oliguria and erythema followed by desquamation. Other authors, however, have not noticed these complications, even when using large doses (see Levrat and Bayeux above). We may therefore assume with some justification that these secondary effects were due, not alone to sodium cacodylate itself, but to the impurities it contained. We would not say that a chemically pure sample of cacodylate might not occasionally give rise to secondary effects of a more or less unpleasant nature, for what active drug is invariably free from such? Instances of idiosyncrasy may occur, but

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\*) See Handlexikon der tierärztlichen Praxis by G. Uebele 1910, p. 350.

Marchal, *Revue vétérinaire* 1903, p. 709.

Brunet, *Recueil de médecine vétérinaire militaire* 1908, p. 860.

Lanceleur, *Revue vétérinaire militaire* 1910, p. 461. — *Clinica veterinaria* 1910, p. 708.

Gautier, *Revue de thérapeutique* 1901, p. 567.

Balzer-Griffon, *Semaine médicale* 1897, p. 266. — *Presse médicale* 1897, p. XXV.

do not justify the abandonment of a drug which has given good results in many cases, as the foregoing remarks have shown.

It is clear that inferior preparations were on the market, for a report appeared by E. Barbano in which it was advised that the strongly alkaline sodium cacodylate of commerce should be carefully neutralised before use by means of cacodylic acid. Such preparations ought not to be used on any account for it may be presumed that in other respects they are below the requisite standard of purity, apart from possessing an alkaline reaction\*). Not only should a reliable preparation of cacodylate be used, but the contra-indications for the use of the cacodylates should be particularly studied. Among these Gautier mentioned liver insufficiency in general, and described the symptoms of intolerance shown by certain patients. These symptoms may be prevented, however, by strict attention to dosage, the important point being to commence with moderate doses, increasing them gradually, and to avoid prolonged treatment without intermissions. In case symptoms of intolerance occur, e. g., conditions of congestion and excitation, abdominal pain, urticaria, humming in the ears and metrorrhagia, this should be taken as a sign that the doses used have been too large. The treatment must then be interrupted and recommenced, say a week later, with smaller doses. In pulmonary tuberculosis hæmoptysis has been given by several authors as a contra-indication. This has already been mentioned.

We must now give a more detailed account of the therapeutic use of other cacodyle preparations, for so far sodium cacodylate has been considered alone. After it iron cacodylate is the most important.

### Ferri cacodylas.

Ferric cacodylate was first described in detail by Gilbert and Lereboullet. They suggested the use of

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Barbano, Bollettino chimico farmaceutico 1907, p. 8.

\*) For the chemical tests for sodium cacodylate see Merck's "Prüfungsvorschriften für die pharmazeutischen Spezialpräparate" 1906, p. 32.

Gautier, Merck's Reports 1901, p. 33.

Gilbert-Lereboullet, Revue de thérapeutique 1900, p. 571.



the preparation in particular for subcutaneous treatment in place of other salts of iron, for its use caused neither unpleasant general symptoms nor renal complications as is sometimes the case with the usual salts of iron. Ferric cacodylate appears particularly indicated for combating a reduction in the number of red blood corpuscles and a diminution in the hæmoglobin in the blood. In chlorosis the preparation causes a rapid, considerable and permanent rise in the hæmoglobin, and this refers equally to various forms of chloro-anæmia, even the chloro-anæmia of phthisis being benefited in its initial stage. In such cases the remedy never causes congestion or hæmorrhage. Even when albuminuria is present the use of ferric cacodylate is not contra-indicated, for the authors have noticed an improvement to follow in several instances. The various forms of leucæmia and lymphadenitis which are amenable to arsenium treatment appear particularly suitable for treatment with ferric cacodylate. It may be given internally or subcutaneously. The doses used by the above-named authors were, for internal administration 0.05 to 0.3 gramme ( $\frac{3}{4}$ —5 grains) daily, and for subcutaneous application 0.03 to 0.1 gramme ( $\frac{1}{2}$ —1 $\frac{1}{2}$  grains). For subcutaneous use they consider that dilute solutions should always be used, for more concentrated solutions may produce local inflammation. They give the following prescriptions:

Rp. Ferri cacodyl.                    0.3 gramme (5 grains)  
Aq. destill. steril.            10.0 grammes ( $\frac{1}{3}$  oz)  
M. Sig.: 1 to 3 c.c. (17—50 min.) to be injected daily.

For internal use they prescribe:

Rp. Ferri cacodyl.                    1.0 gramme (15 grains)  
Aq. Cinnamom.                    25.0 grammes ( $\frac{5}{8}$  oz)  
M. Sig.: 20 to 40 drops to be taken 3 times a day.

Fiora prepared a solution suitable for subcutaneous injection, and stated by him to be very stable, according to the following directions: 1 gramme of ferric cacodylate and 0.6 gramme of sodium citrate are dissolved in a mixture of 1 part of glycerin and 4 parts of water, so that the volume of the solution amounts to 5 c.c.

Senator also regards ferric cacodylate as an excellent

remedy in anæmia, no matter whether it be given internally or subcutaneously. He recommends the latter mode of administration particularly when the internal use is contra-indicated because of gastric ulcers. The preparation also gives excellent results in severe diseases of the blood, such as pernicious anæmia and hæmorrhagic diathesis, for it contributes to the relief of the subjective symptoms and to an increase in weight. G. Lalli was extremely satisfied with the action of ferric cacodylate in the treatment of anæmia and chlorosis in children. He found it to increase the colouring matter of the blood and the red blood corpuscles, while it had a very beneficial effect on metabolism and on the general condition.

E. Franck refers to the intravenous use of ferric cacodylate. He used a sterile solution of the following composition put up in glass ampoules:

Rp. Ferri cacodyl. 0.05—0.1 gramme ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains)

Aq. destill. 1.0 —2.0 grammes (17—34 min.)

The contents of one ampoule are injected every day or every other day intravenously, for this mode of application, when properly carried out, causes no pain. It is best to commence with the smallest dose, and to increase it after a few injections to 0.075 or 0.1 gramme ( $\frac{1}{6}$ — $1\frac{1}{2}$  grains). A series of 30 injections is usually enough. It is advisable, however, not to break off the treatment abruptly, but to continue giving a dose twice a week. This form of treatment is especially useful in anæmia and chlorosis when internal administration of the remedy is not suitable, as in organic diseases of the stomach, in hyperacidity and hypersecretion, and in cases where dyspeptic troubles are aggravated by the use of iron. It is also indicated in the case of bedridden patients, to hasten convalescence. Finally it appears to be of practical use and desirable in certain combinations of diseases in which it is necessary to prevent the admixture of iron with other drugs that are being administered internally. An example of this form of disease is a case in which late syphilis is suspected and glandular swellings develop with great rapidity. By the internal administration of iodine and the intravenous application of

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Lalli, La Pediatria 1901, No. 9 and 10.

Franck, Medizinische Klinik 1906, p. 566. — Merck's Reports 1906, p. 4.

ferric cacodylate it is often possible in these cases to check the swelling of the glands or to cause such swellings to subside. The maximum dose injected by the author in a case of this kind was 2 grammes (34 min.) of a solution of 1:25:20:0. In chronic malaria the internal administration of quinine is recommended in combination with the intravenous use of ferric cacodylate (maximum dose 2 grammes of a 1:10 solution).

### Guaiacol cacodylas.

This preparation is used almost exclusively in the treatment of tuberculosis. For internal administration it is not to be recommended, for it contains too small a proportion of guaiacol for this purpose. Hence, those who desire to administer guaiacol and cacodylic acid *per os* would do better to use a combination of guaiacol with sodium cacodylate mixed in suitable proportions. Guaiacol cacodylate is very well suited, however, for subcutaneous and intramuscular application. It was first used by Barbary and Rebec for subcutaneous injection in an oily solution. They report excellent results with it in tuberculosis. A solution of 0.05—0.1 gramme ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains) of the preparation in 1 c.c. (17 min.) of sterile olive oil is used, this dose being injected every other day. Burlureaux recommends a 5 p.c. aqueous solution for subcutaneous and intramuscular application, 1 c.c. being injected every two to three days. If a small quantity of pure guaiacol be added, the author states that the solution will not become turbid, moreover, this addition gives the solution a slight anæsthetic action. In tuberculosis with fever these injections are of advantage, for they reduce the fever, diminish the expectoration and excite the appetite. They are also said to be of considerable service in influenza in which 1 or 2 injections frequently cause a rapid fall of temperature. They are also valuable during convalescence from influenza.

G. Menusier considers cases of tuberculosis in which the disease is due to hereditary predisposition to be partic-

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Barbary-Rebec, Bulletin médicale 1901, p. 741. — Bulletin des sciences pharmacologiques 1900, p. 4.

Burlureaux, Union pharmaceutique 1906, No. 3. — Presse médicale 1906, p. 31.

Menusier, Médecine orientale 1902, p. 231.



ularly suitable for treatment with guaiacol. He injected 3 c.c. (50 min.) of a 5 p.c. aqueous solution every 4 days.

After the value of cinnamic acid in the treatment of tuberculosis became known, a combination of it with cacodylic acid was tried. Astruc and Murco describe a preparation of this kind, the so-called cacodyle cinnamic acid. It forms white prisms, soluble with difficulty in ether, glycerin and fatty oils, but readily soluble in alcohol. It is said to be decomposed by water into its components (cacodylic acid and cinnamic acid). The authors give to the preparation the chemical formula  $C_6H_5 \cdot CH:CH \cdot COOH \cdot AsO(CH_3)_2 \cdot OH$ , but it must be merely a mechanical mixture, in molecular proportions, of cacodylic acid and cinnamic acid.

#### Hydrargyri cacodylas.

With regard to the therapeutic use of mercuric cacodylate, we have communications by Vajas, Brocq, Giuffo, Jullien and Berlioz. The significance of the papers is merely relative, for there is no way of ascertaining how the preparations were made, and what degree of purity or impurity they possessed. Vajas made pharmacological investigations which showed that the mercuric cacodylate used by him caused no local inflammation. The lethal dose for rabbits was 0.8 gramme per kilogramme of rabbit. Doses of 0.02—0.06 gramme ( $\frac{1}{3}$  to 1 grain) were always followed by a gain in weight. Intravenously the cacodylate had a more toxic action, but it was tolerated by these animals in doses of 0.02—0.05 gramme without injury. Vajas also made a clinical trial of mercuric cacodylate, and regards 0.03 gramme ( $\frac{1}{2}$  grain) as the normal daily dose of the preparation. Jullien and Berlioz speak very favourably of the value of mercuric cacodylate in syphilis, particularly as it agrees very well with the patients. They gave doses of 0.01—0.02 gramme ( $\frac{1}{6}$ — $\frac{1}{3}$  grain). Equally favourable results were obtained by Giuffo, who gave subcutaneous injections of 1 c.c. of a

Astruc-Murco, *Journal de pharmacie et de chimie* 1900, II., p. 553.

Vajas, *Bulletin de la société de biologie* 1900, May 25.

Brocq, *Revue de thérapeutique* 1901, p. 537.

Giuffo, *Riforma medica* 1903, No. 3.

Jullien-Berlioz, *Nouveaux remèdes* 1903, p. 223.

2.5—5 p.c. solution of mercuric cacodylate daily for 15 to 30 days.

Using hydrargyri cacodylas “Merck”\*) doses may be given daily of 1—2 c.c. of a 5 p.c. aqueous solution, subcutaneously or intragluteally. 1 c.c. of this solution corresponds to about 0.0115 gramme Hg=0.0125 gramme HgO=0.0261 gramme HgI<sub>2</sub>. If desired, this solution may be combined with sodium cacodylate and cocaine hydrochloride.

### Hydrargyri iodo-cacodylas.

A definite chemical preparation worthy of the name of mercuric iodo-cacodylate does not as yet exist; at any rate no such compound has been prepared from iodo-cacodylic acid\*\*). The solutions which have been given the above name are combinations of cacodylic acid and iodide of mercury, or of salts of mercury and iodine. These combinations have been used because it is not yet possible to prepare mercuric cacodylate of sufficient purity and of high enough percentage, and because the preparations that have so far been issued are said to give rise to pain when injected subcutaneously. For this reason Ciavette and Fraisse among others recommend the following solution in place of mercuric cacodylate: 1 gramme of mercuric cacodylate\*\*\*) and 2 grammes of cacodylic acid are dissolved in 75 grammes of distilled water. Another solution is prepared consisting of 1 gramme of sodium iodide in 5 c.c. of water. This solution is added to the former. It is then neutralised with dilute caustic soda, and the mixture is made up to 100 c.c. with water. This solution keeps well and may be sterilised. Each cubic centimetre contains 0.01 gramme of mercuric cacodylate, equivalent to about 0.01 gramme of biniodide of mercury. For the treatment of syphilis 1 c.c. of this is injected into the glutei every other day. This treatment may be continued for 2—3 weeks, when an interval of 8—10 days must be allowed. If the injections are well borne the doses may be increased to 2 c.c. each. The authors regard this treatment as indicated

\*) See p. 3.

\*\*) For iodo-cacodylic acid see: Auger, Comptes rendus de l'Académie des sciences Vol. 146, p. 1280.

Ciavette-Fraisse, Presse médicale 1901, p. 23 and 26, 1902, 626. — Revue pratique des maladies cutanées, syphilitiques et vénériennes 1902, No. 3.

\*\*\*) Or 2 grammes of Hydrarg. cacodyl. Merck.

in syphilis with depression, neurasthenia and wasting, in syphilis with dermatoses and in obstinate syphilis maligna præcox resembling acne, especially if other methods of treatment have failed. The results of this treatment were extremely satisfactory in Ciavette and Fraisse's experience, the symptoms being promptly relieved in the majority of cases. Good results were also obtained with this solution<sup>1</sup> by Tommasi and G. Löwenbach. The latter, in preparing his solution, started from mercuric oxide which he dissolved in an excess of cacodylic acid, whereupon he used the mercuric cacodylate which separated out in the manner described above. As the result of many trials he recommends the use of solutions of mercuric iodo-cacodylate particularly in cachectic anæmia, and in persons with ulcerous and gummatous lesions in the early or late stage of syphilis, even if other forms of treatment with iodine and mercury have failed. The treatment is also indicated in the polymorphous early stages, in the later papulo-squamous and lichen forms, and in syphilis combined with psoriasis. In cases of slight syphilis in well nourished persons, this treatment is said to be useless.

Troussaint gives the following directions for the preparation of a solution of mercuric iodo-cacodylate:

Rp. Hydrarg. biniod.	0.01 gramme
Sod. iodid.	0.02 „
Sod. cacodyl.	0.05 „
Aq. destill.	1.0 „

The author used this solution in the treatment of a typical case of pulmonary syphilis, giving three series of 7 injections at equal intervals, with the simultaneous use of tonics. The general condition and the local appearances improved very quickly, the phlegm and cough left off, and after a month no physical signs could be elicited by the stethoscope.

### Magnesium cacodylas.

Magnesium cacodylate was recommended by Burlureaux for the same indications as for sodium cacodylate,

Tommasi, *Giornale internazionale delle scienze mediche* 1902, p. 641.

Löwenbach, *Therapeutische Monatshefte* 1903, p. 480.

Troussaint, *Marseille médical*, June 1, 1904.

Burlureaux, *Bulletin de thérapeutique* 1901, p. 524.



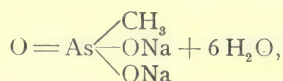
using subcutaneous injections. It is very readily soluble, and contains relatively more cacodylic acid. Neither of these properties, however, render its use more advantageous than that of sodium cacodylate which is also readily soluble. Burlureaux began his investigations with a 10 p. c. aqueous solution, using doses of 0.5—1 c. c. He continued this treatment with a 25 p. c. solution. When the anæsthetic action of the magnesium salts has become better known, magnesium cacodylate may perhaps assume greater importance in therapeutics.

### *Strychninæ cacodylas.*

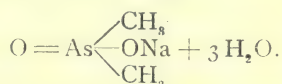
This preparation also has as yet gained no therapeutic importance. Eysseric used it in the treatment of tuberculosis; and came to the conclusion that its action was due rather to its strychnine content than to the cacodylic acid, for it contains but little of the latter. Strychnine cacodylate has a specially good effect upon the appetite, and thus upon the general condition. It is given subcutaneously, starting with a dose of 0.002 gramme ( $\frac{1}{32}$  grain) a day, increasing rapidly to 0.02 gramme ( $\frac{1}{3}$  grain) while the treatment is concluded with doses varying between 0.02 to 0.03 gramme ( $\frac{1}{3}$ — $\frac{1}{2}$  grain). A solution for injection is prepared by warming 10 grammes of glycerin on a water bath, and dissolving 1 gramme of the preparation in it, when it is made up to 100 c. c. with water. 3.5 c. c. may be taken as the maximum dose.

### *Sodii monomethyl-arsenas.*

This preparation may be mentioned here because it is very closely allied chemically to sodium cacodylate. It is derived from monomethyl-arsenic acid so that it contains one methyl group less than dimethyl-arsenic acid (cacodylic acid). It has the following constitutional formula:



that of sodium cacodylate being



Sodium monomethyl-arsenate (methyl di-sodium arsenate, arsinal, arrhenal) is a white, crystalline powder soluble 1 in 2 of water. It was introduced into therapeutics by Gautier, and is said by him to be better suited for internal treatment than sodium cacodylate. He has used it with excellent results in tuberculosis, asthma, emphysema, chorea, intermittent fever, and, subcutaneously, in paludism and hyperemesis gravidarum. Other communications have been published by Thébault, Bolognesi, Stahl, Lemanski, Fontoynt, Guérin, Vajas, Vigenaud, Chaumier, Cochez, Laveran, Chassevant, Mouneyrat, Gallo, Variot and Bonsignorio. These papers show that the results obtained with methyl-di-sodium arsenate, whether used internally, externally or subcutaneously, the indications for its use and the dosage are identical with those of sodium cacodylate, therefore only some of the original prescriptions need be reproduced here.

Variot uses the following prescription in children to aid nutrition and growth:

- Gautier, *Comptes rendus* 1902, Vol. 134, p. 329. — *Presse médicale* 1902, p. 201, 260 and 1259. — *Semaine médicale* 1902, p. 59. — *Bulletin médical* 1902, p. 191. — *Revue de thérapeutique* 1902, p. 149 and 1903, p. 123.
- Thébault, *Bulletin général de thérapeutique*, August 30, 1902. — *Revue de thérapeutique* 1902, p. 713.
- Bolognesi, *Nouveaux remèdes* 1902, p. 289.
- Stahl, *Thèse de Paris* 1902.
- Lemanski, *Revue internationale de médecine* 1902, p. 147.
- Fontoynt, *Presse médicale* 1902, p. 824, 1903, p. 240.
- Guérin, *Presse médicale* 1902, p. 620 and 791. — *Revue de thérapeutique* 1902, p. 442.
- Vajas, *Thèse de Paris* 1902.
- Vigenaud, *Revue de thérapeutique* 1902, p. 408.
- Chaumier, *Presse médicale* 1902, p. 620. — *Revue de thérapeutique* 1902, p. 436.
- Cochez, *Presse médicale* 1902, p. 822. — *Revue de thérapeutique* 1902, p. 699.
- Laveran, *Presse médicale* 1902, p. 1260, 1903, p. 60. — *Revue de thérapeutique* 1903, p. 86.
- Chassevant, *Revue de thérapeutique* 1902, p. 409 and 696.
- Mouneyrat, *Journal de pharmacie et de chimie* 1902, p. 442.
- Gallo, *La Pediatria* 1907, p. 869. — *Revue de thérapeutique* 1908, p. 285.
- Variot, *Klinisch-therapeutische Wochenschrift* 1908, p. 1438.
- Bonsignorio, *Presse médicale* 1908, p. 246.

Rp. Sod. monomethylarsen.	0.1 gramme ( $1\frac{1}{2}$ grains)
Aq. destill.	100.0 grammes ( $3\frac{1}{3}$ oz)
Syrup. Cinchon.	50.0 „ ( $1\frac{2}{3}$ oz)

Children of 6 months to 2 years are given 1 to 2 teaspoonfuls after the midday meal, children of 2—4 years 1 tablespoonful, and children of 4—8 years 2 dessertspoonfuls. Should the patient's skin assume an odour of garlic, the treatment should be continued for not more than two weeks when an interval of 2 to 3 weeks should be allowed.

Trébault prescribes it as follows:

Rp. Sod. monomethylarsen.	5.0 grammes (75 grains)
Aq. Menth. pip.	100.0 „ ( $3\frac{1}{3}$ oz)
10 drops to be taken after meals.	Maximum dose 25 drops a day.

Rp. Sod. monomethylarsen.	0.08 gramme ( $1\frac{1}{4}$ grains)
Extract. Opii	0.04 „ ( $\frac{2}{3}$ grain)
Syrup. Citri	40.0 grammes ( $1\frac{1}{3}$ oz)
Aq. Tiliæ	125.0 „ (4 oz)

Sig.: 5 tablespoonfuls to be taken daily.

For the treatment of essential asthma:

Rp. Sod. monomethylarsen.	0.05 gramme ( $\frac{3}{4}$ grain)
Syrup. Bellad.	30.0 grammes (1 oz)
Syrup. Opii.	30.0 „ (1 oz)
Aq. Menth. pip.	125.0 „ (4 oz)

Sig.: 1 tablespoonful to be taken every 2 hours.

For subcutaneous use a 5 p.c. aqueous solution is employed, of which of 0.5 to 2 c.c. may be injected daily.

In the presence of hæmoptysis, or disease of the liver, the use of this preparation must be carefully supervised by the physician.



## KEPHIR.

On the northern slopes of the Caucasus, and apparently in the steppes of Siberia, a drink has been prepared and consumed for ages which consists essentially of fermented mares' milk\*). This is known as "koumiss". This drink is said to be still one of the chief foods of the natives of the Caucasian steppes. As it can only be prepared in summer, i. e., only in the warm season when the temperature is sufficiently high to permit of the fermentation of milk, the use of koumiss is restricted, in the case of the dwellers in the steppes, to the summer. It is said that the people waste in the winter, though this is possibly due to the worse conditions of life in general in winter, while in the summer, when they obtain regular or exclusive supplies of koumiss, they become again well nourished and strong. This state of affairs led to the introduction of kephir into therapeutics, particularly for the treatment of pulmonary tuberculosis\*\*). The treatment may thus have been founded on fact, on insufficient observation, or on the high opinion which the Caucasians themselves hold of koumiss.

The value of koumiss became known in the middle of the last century, and the fact came to light that consumptive persons in the Caucasus were cured by means of koumiss, or in other cases obtained great relief from their sufferings. The people of the West then became interested in this remedy. A circumstance that prevented its rapid spread was the fact that the ferment used by the Caucasians in the

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\*) According to Herodotus, the Scythians of the lower Danube were familiar with the preparation of milk wine.

\*\*) See Stahlberg, *Der Kumys, seine physiologischen und therapeutischen Wirkungen*, 1869. — Kisch, *Erfahrungen über den Kumys*, *Prager Vierteljahresschrift für praktische Heilkunde* 1873. — A. Karrick, *Kumys und seine Anwendung bei Lungenschwindsucht*, *Petersburg* 1882. — Georgiewski, *Russkij Wratsch* 1883. — Stange, *Über Kumyskuren* 1883. — Goldhausen, *Kumys (Milchwein) als Heilmittel*, *Halle a. S.* 1889. — Dimitrieff, *Journal de pharmacie* 1885, p. 562. — Maximow, *Semaine médicale* 1884, No. 8. — Krakauer, *Wiener medizinische Presse* 1898, No. 4. — Thymowski, *Physiologische und therapeutische Bedeutung des Kumys*, *München* 1877. — Sklotowski, *Russkij Wratsch* 1883, p. 715.

preparation of koumiss was unknown, and could not be obtained commercially, for the Mohammedan people of the Caucasus believe that the ferment "kephir" or "kapir", also known as "The Prophet's millet" would lose its power if unbelievers participated in the blessings of the remedy. For this reason the preparation of the kephir ferment was more or less shrouded in mystery for a long time.

The Mohammedans relate that Mohammed himself left grains of kephir to true believers as a gift. Others regard it as a direct gift of God, God having presented the kephir grains and made known the way to use them to an old man as a reward for his faith, in the time in which he consorted in person with the founders of the race. It is said that for a time the transfer of kephir grains was forbidden. Goldhausen attributes the origin of the use of kephir by the Asiatic natives to the Kumanes, who are mentioned in the writings of Xenophon and Pliny. When the Kumanes were conquered by the Tartars (1215) the preparation and use of kephir wine is said to have been taken up by the victors. The word "koumiss" is derived from the Kumanes.

The word "kephir" is probably derived from the Turkish "kef" or "keyf" signifying "well-being", for after taking kephir milk (kephir wine) it is said that a decided feeling of well-being is experienced. The word kephir is now applied not only to the ferment, the kephir grains, but also to the drink prepared with it: kephir milk. The latter is distinguished from koumiss by the fact that it is prepared, not from mares' milk, but from cow's milk. The name "koumiss" has also been given, with some justification, to a substitute for kephir milk prepared, in default of sufficient genuine kephir ferment, from milk, sugar and beer yeast. Of course a drink thus prepared does not correspond in its composition and properties with kephir when properly prepared, and kephir appears to have almost completely supplanted the koumiss prepared from sugared milk with the aid of yeast. It should be remarked that there are other drinks allied to kephir, but their preparation is seldom undertaken in Western Europe. Thus the Armenians prepare a drink from buffalo milk; it is called Madzonn and corresponds to the Bulgarian Yoghourt\*).

\*) See C. Wegele, Deutsche medizinische Wochenschrift 1908, p. 11.

Koumiss is first mentioned in the reports of the French monk William Rubriquis (Rubruck) who travelled in the Caucasus as a missionary in the middle of the 13<sup>th</sup> century. It was mentioned again by Marco Polo in the reminiscences of his travels. Marco Polo, in the year 1271, visited Kublai, then Chan of the Tartars, and travelled in the land of the Tartars for more than 20 years under his protection. For 500 years koumiss was not again mentioned in our literature, and we have to wait for the year 1788 before a fairly accurate description was given by J. Grieve, while in 1811 it was recommended by Heberlein in pulmonary consumption. 47 years later Postnikoff erected the first Sanatorium for the treatment of pulmonary affections in which the patients were systematically treated with kephir. Kephir became more generally known through the publications of Sipowitsch in the year 1867, and by the first Kephir Cure Institute erected in the year 1881 by Dimitrieff in Jalta (Crimea).

The first institute for the preparation of kephir on a large scale was founded by Stahlberg in 1874 in Vienna. In his determination to supply the patient with an absolutely unadulterated koumiss this physician obtained a large number of mares from the Steppes, and engaged Kirghizes of great experience for the preparation of the milk wine. The use of mares' milk was soon abandoned, however, for it was found to possess no greater therapeutic value than cow's milk, while Biel and Landowsky proved by analysis that the koumiss derived from it could scarcely be distinguished in its composition from cow's koumiss.

Before turning to a consideration of the medical properties of kephir, its preparation and properties must be briefly considered from the biological, chemical and physiological points of views.

The Caucasians have always prepared their kephir or koumiss in leathern bags (Burdjuk - Kephir\*) about the walls of which in the course of time a kind of fungus

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Marco Polo, see R. Stuebe, *El libro*, Leipzig 1902 and Bürck, Leipzig 1855.

Grieve, Account of the method of making Koumiss by the Tartars with observations on its use in medicine. Edinburgh 1788. Dimitrieff, Kefir, Hannover 1884.

\*) See Ssadowen, *Russkij Wratsch* 1883, p. 135.



crust forms as a result of the continual fermentation. This is removed from the walls by scraping, and is dried at ordinary temperature in an airy place. The dry residue thus obtained constitutes the kephir grains of commerce. They form yellowish-grey nodules with a peculiar, faint odour. When softened in water or milk they exhibit the property of causing milk to ferment, producing a specific change which will be described presently.

An investigation of the active substances and micro-organisms responsible for this change has been carefully carried out by various workers. E. Kern attributes the change of milk into kephir milk or into kephir principally to a micro-organism which he names *Dispora Caucasica* because it is a rod-shaped fungus having two little bodies which resemble spores at its two ends. The hypothesis, however, that the above-named bacterium is the active constituent of kephir, was abandoned by Sorokin, who advanced the opinion that the kephir grains consist principally of yeast and *leptothrix*, but even this hypothesis rests on an insecure footing, for W. Beyerinck found in his investigations that commercial kephir contains a form of yeast which differs from ordinary beer yeast. He named it "*Saccharomyces Kephir*"\*). He regards Kern's *bacillus* as an active living agent. In his opinion this *bacillus* (the *Dispora Caucasica* Kern) effects the transformation of sugar of milk into lactic acid, while the *saccharomyces* gives rise to a ferment which converts sugar of milk into galactose. This ferment was named by him "lactase". A tryptic ferment is said by him to be also produced by this *saccharomyces*, but this ferment is not identical with *pepsin*. The conclusions which Beyerinck drew from his investigations are striking. He considered it advisable to breed the two organisms separately, the *Dispora* and the *saccharomyces*, and allow them to act separately on the milk. The products of the two reactions should then be mixed before being taken. He believed that the same result might even be obtained by means of a mixture of milk, alcohol

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Kern, Bulletin de la société impériale des naturalistes de Moscou 1881, No. 3.

Beyerinck, Niederländisches Archiv für Heilkunde 1889, p. 428.

\*) Arcangeli called it "*Saccharomyces minor*". (Milchindustrie 1889, p. 130.)

and carbonic acid as with kephir milk. It is obvious that this suggestion could lead to no good results. No expert in matters of diet would support a procedure in direct opposition to our present views at a time when we are careful to avoid branding mixtures as fermented drinks or to give them by artificial means the appearance of fermented drinks. A substitute for kephir milk of very doubtful value was at one time recommended by Levy. As reported by Weiss, Levy was of opinion that a fermentation peculiar to kephir fermentation could be produced in milk by taking one part of ordinary sour milk and nine parts of boiled milk and mixing them by frequent shaking at a temperature of 12° R. So doubtful a substitute for kephir as this preparation has been condemned by Weiss, Monti, Herz and Kobert.

Struve came to the conclusion that the fermentative action of kephir is due to the presence of *saccharomyces mycoderma*. He attributes the formation of kephir ferment to a special process in the growth of this yeast fungus in the connective tissue of the leathern bags, an important factor being the impeded liberation of carbonic acid in the process of fermentation. The proof of this statement, however, could not be given for want of suitable kephir bags like those used by the Caucasians.

With regard to the *Dispora Caucasica* the views of Podwyssotzki are of some interest. He considers this bacterium to be allied to the hay fever bacillus, and supposes that the formation of kephir ferment in the olden days occurred because the hay bacillus present in large quantities in the fields and downs had found its way into the milk of goats and other animals of the nomad tribes of that time, and had gradually adapted itself to the new nutrient medium. In this way a bacterium was created that was partic-

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Weiss, Schitzlers Zeit- und Streitfragen. Vienna 1890, p. 387.

Monti, Wiener medizinische Zeitung 1887, No. 22.

Herz, Deutsche Praxis, 1902, p. 615.

Kobert, Zeitschrift für Krankenpflege 1904, p. 380.

Struve, Berichte der deutschen chemischen Gesellschaft 1884, I., p. 1364.

Podwyssotzki, Zeitschrift für diätetische und physikalische Therapie, Vol. 5, No. 7 and 8.

Podwyssotzki, Le Képhir, ferment et boisson thérapeutique préparé avec du lait de vache. Paris 1902.

ularly well suited for symbiosis with the other bacteria commonly occurring in milk.

E. von Freudenreich shows that all the investigations of kephir prove that in the kephir ferment a symbiosis of several micro-organisms is present. Among these is a kind of yeast which has not the power of fermenting sugar of milk without the aid of other micro-organisms, a lactic acid bacillus and Kern's bacillus, already mentioned as having been grown by Beyerinck, the *Dispora Caucasia*. Freudenreich confirmed Kern's statements in his own experiments, though he does not regard the granules occurring at the ends of this bacillus to be spores, as assumed by Kern. Hence he altered the name "*Dispora Caucasia*" into "*Bacillus Caucasicus*". In the kephir milk preparations made by the author he usually found four different micro-organisms: yeast cells, cocci in chains, smaller cocci and bacilli. The kephir yeast was found by him to cause no fermentation in milk, in which, however, it grows well, and gives rise to a peculiar taste. The most favourable temperature for its growth is 22° C. In Freudenreich's opinion it cannot be regarded as identical, from a morphological and biological point of view, with ordinary beer yeast, as is frequently stated. The large streptococcus in chains (streptococcus a) causes the formation of lactic acid, but it is not so productive as the small coccus (streptococcus b). It is the latter which acts together with kephir yeast in causing the fermentation of sugar of milk. The bacillus *Caucasicus* also takes part in the lactic acid fermentation.

By means of experiments with pure cultures of these kephir organisms Freudenreich proved that all these micro-organisms are as a rule concerned in the production of kephir milk. This was only possible by the united action of the four microbes, although occasionally it might occur in the absence of the bacillus *Caucasicus*. The rôle of the latter organism is not quite clear. It will probably prove to be of chief importance in providing a means of distinguishing genuine from non-genuine kephir, for it is certain that it is never absent from genuine kephir grains. Freudenreich believes, however, that the streptococci may occasionally be replaced by other cocci of similar action even in genuine kephir.



Eckervogt explains the fermentation which takes place under the influence of the kephir fungus as follows: "Part of the milk sugar is converted into lactic acid by the lactic acid fungus which is contained in kephir grains. Another part of the milk sugar takes up water, probably as the result of the action of the Caucasian fungus, and is thus converted into a substance capable of undergoing fermentation. This is transformed into alcohol and carbonic acid by the yeast which is likewise present in kephir grains. The lactic acid thus formed tends to cause the casein to precipitate, for casein cannot remain in sour milk. It does not clot in thick masses, however, but comes down in very small flakes in close association with the minute droplets of fat in which it is inclosed (herein lies the value of the action of the Caucasian fungus). At the same time part of it becomes fluid and is converted into hemi-albumose and peptone". Thus Eckervogt attributes a specific action to the *Bacillus Caucasicus* and regards it as the essential constituent of kephir.

We must admit that the action of the kephir organisms and their special functions in the fermentation of kephir milk has not as yet been fully explained\*), and we cannot yet say with certainty which of the organisms is responsible for the formation of albumoses and of more or less peptonized albumins. We may regard it as established, however, that the alcohol contained in fermented kephir is a product of a *saccharomyces*, while the lactic acid it contains is the product of the *Bacillus Caucasicus*, or of the common lactic acid bacillus.

Attempts have also been made to ascertain the constituents of kephir grains analytically, although the nature of kephir cannot be explained in this way. Struve found that dried kephir contained about 11 p. c. of water, 4 p. c. of fat, 11 p. c. of soluble substances resembling peptone, 10 p. c. of protein bodies soluble in ammonia and 30 p. c. soluble in caustic potash, and 33 p. c. of insoluble residue. The latter was found to be a mixture of *Saccharomyces* and *Bacillus Caucasicus* with small quantities of *Leptothrix* and *Oidium lactis*. We have better information as to the composition of the perfectly fermented kephir

\*) See J. König, *Die menschlichen Nahrungs- und Genußmittel*, Berlin 1904, p. 744.

milk. The action of the combination of fungi on milk leads to the formation, according to the duration of the action and the temperature, of varying proportions of alcohol, carbonic acid, lactic acid, hemi-albumoses, albumoses and peptones. Kephir two days old contains about 1 to 1.5 p. c. of alcohol, 2 p. c. of unaltered sugar, 1 p. c. of lactic acid, 1 p. c. of albumin, 0.3 p. c. of salts, about 1 p. c. of carbonic acid, and in addition fat in the proportion in which it was present in the original milk. Kephir one day old contains less alcohol and carbonic acid, while kephir 3 days old contains more. Naturally the composition of the milk used in the preparation of kephir is an important factor which influences the result. The formation of acid and of carbon dioxide which occurs during fermentation leads to the separation of the milk albumin for the greater part in extremely fine subdivision. A white, translucent fluid is formed with an agreeable slightly acid and refreshing taste. Another part of the milk albumin is peptonized, and Stern states that at a particular temperature the whole of the casein may be transformed into peptone. Exhaustive investigations into the changes which take place in the milk albumin under the influence of kephir ferment were undertaken by Biel. He found that in kephir fermentation there were formed from the casein not merely products which could not be precipitated by acids, but others which are far more readily digestible than unaltered milk albumin. Thus it is at any rate certain that kephir is a drink which contains all the nutritive substances of the milk, and contains them in a form in which they are well borne by the stomach, even if debilitated. This is obvious from the circumstance that the kephir fluid is no longer capable of being precipitated by acids, so that in the stomach there is no separation of lumps of almost indigestible casein. More than that, properly prepared kephir, particularly in the hot season, forms a refreshing drink with an agreeable taste. It is no wonder, therefore, that kephir has become a favourite drink with both young and old, healthy and ill, and is recognized as a dietetic remedy of the greatest importance.

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Stern, Deutsche medizinische Wochenschrift 1885, No. 11.

Biel, Petersburger medizinische Wochenschrift 1885, No. 17.

With regard to the physiological properties of kephir milk, the following statements may be made: In small quantities kephir causes an increase in the appetite, while if taken in large quantities all other food may be dispensed with for weeks and months. Even invalids may be fed for weeks exclusively on kephir. Kephir contains so little alcohol that it has no exciting action, but it causes an agreeable feeling of warmth in the stomach, increases the desire for drink, improves the functions of the skin, of the kidneys, and of the heart, increases respiration, stimulates the nerves, favours the deposition of fat in the organism, and diminishes the secretion from the mucous membranes. Stahlberg found the alcohol contained in kephir to favour the formation of fat, while it lowered the temperature of the body and promoted sleep. The sugar of milk increases the weight of the body, the lactic acid reduces the pulse-rate, diminishes the secretion from the mucous membranes, and causes a refreshing, cool feeling. Casein is an albuminous substance which restores the organic tissues, while the carbonic acid causes slowing of the cardiac contractions. Further, it increases the force of the heart, and has a diuretic action\*). Chomenkoff states that the use of kephir milk improves the condition of the blood, making it richer in fibrin and hæmoglobin. Seeland considers kephir of equal value to the transfusion of blood. Theodoroff came to similar conclusions in his study of the effect of kephir treatment on metabolism. The most important result of his investigations is that the digestive activity is materially improved, even in very weak conditions of the digestive organs, with the result that the nutrition is improved and the patient sleeps better. He also observed a considerable increase in the number of red blood corpuscles. These results are partially in agreement with those of May's investigations, which showed that kephir is more digestible than milk. The more perfect digestion of kephir

\*) The increased diuresis is thought by Georgiewski (l. c.) to be due, not to the specific action of kephir, but to the increase in the amount of fluid taken. A specific diuretic action, such as other authors describe, does undoubtedly occur, for sugar of milk is a well known diuretic.

Theodoroff, Verhandlungen der physikal. - medizinischen Gesellschaft in Würzburg, Vol. 19, No. 4.

May, Annalen der Münchener Krankenhäuser 1895.



is undoubtedly due to the alcohol and lactic acid it contains, perhaps also to its modified albuminous substances (albumoses and peptones). The digestive value and the nutritive value are treated more fully by Hallion and Carrion. As the result of their trials they stated that the micro-organisms of kephir possessed similar digestive properties to those of the gastric ferments. In their opinion kephir therefore relieves the stomach of a great part of its digestive work, and very considerably assists digestion. Moreover it is said to inhibit the development of pathogenic bacteria in the digestive canal, thus protecting the organism from their harmful effects, and finally destroying the toxins present in the intestine. This physiological action of kephir has been mentioned already as having led to its use in pulmonary consumption. Its use in this disease was recognized and described by Heberlein, Postnikoff and Sipowitsch, and has been further investigated by other observers such as Podwyssotzki, Gebhard, Theodoroff, Eckervogt, Weiss, Mandrowski, Ponomaroff and Biel, who have studied its preparation and therapeutic use.

The first therapeutic use of kephir milk, as far as can be historically ascertained, was made in the treatment of pulmonary tuberculosis. At first its value was certainly exaggerated, and no wonder, considering the universally acknowledged benefit produced by it on the general condition of the patients. Thus v. Maydel\*) reports that consumptive patients with cavities were so far restored by kephir as to lead him to doubt whether he had not been mistaken in his diagnosis. He therefore regards kephir milk as the best known remedy for pulmonary consumption. Postnikoff\*) came to the opinion that kephir treatment could

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Hallion-Carrion, Presse médicale 1901, p. 94 and 101.

Podwyssotzki, Über Kefir. Odessa 1884. See Rechtshammer, Therapeutische Monatshefte 1903, p. 258.

Gebhard, Dissertation Würzburg 1885.

Theodoroff, Verhandlungen der physikalischen Gesellschaft Würzburg, Vol. 19, (N.F.), No. 4.

Eckervogt, Kefir und seine Darstellung aus Kuhmilch. Leipzig 1890.

Weiss, Kefir, seine Anwendung und Wirkung, Vienna 1890.

Mandrowski, Deutsche medizinische Wochenschrift 1884, p. 324.

Ponomaroff, Archiv für Kinderheilkunde Vol. 5.

\*) See Goldhausen (Kumys) 1889, p. 8.

prevent the formation of tubercles in the lungs, while it controlled the diarrhœa and the fever, and had a very good effect on cough, expectoration and dyspnœa. These statements were in part confirmed by other authors, such as Gebhard, Löbel, Loewensohn and Feig. However, no physician now regards kephir milk as a specific for tuberculosis. A point of fundamental importance is to use kephir in as early a stage of the disease as possible. There is no doubt that it has far less influence in advanced phthisis, though the little benefit that does result, viz., the improved state of nutrition, renders it of the greatest value even in hopeless cases. It is certainly an important point in the case of a disease like pulmonary tuberculosis to obtain a food like kephir, the taste of which, if properly prepared is agreeable, while it can be taken for long periods without creating a distaste. It is in the first and second stages of tuberculosis, however, that kephir is of invaluable service, as appears from recent reports by Trojanowski. In his experience no remedy can be compared even remotely with cow's koumiss, even in advanced cases. Its principal action is due to a surprisingly rapid improvement in the condition of nutrition which follows its administration, and naturally it is no use giving kephir by tablespoonfuls. The daily consumption should amount to several litres at the least. Thus Trojanowski states that among his patients in the first and second degrees those who had taken 6—7 litres of kephir milk daily for three months were completely cured. When hæmoptysis is present, caution is necessary, for Fleroff found that kephir favours and increases hæmoptysis, and for this reason he declares it to be contra-indicated in these cases.

Even though kephir cannot be regarded as a specific in the treatment of pulmonary tuberculosis, there is a tendency to look upon it as a specific in various gastric and intestinal diseases, for the results described in the literature are entirely favourable. Justification for this state-

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Löbel, Medizinische Klinik 1906, No. 19.

Loewensohn, Therapeutische Monatshefte 1903, p. 212.

Feig, Prager medizinische Wochenschrift 1905, No. 8.

Trojanowski, Wiener medizinische Wochenschrift 1907, No. 13—20.

Fleroff, Russkij Wratsch 1898, No. 3.

ment may be found in the publications of Hallion and Carrion, and it is further supported in the reports of Theodoroff, Mandrowski, Hirsch, Hayem, Löbel, Wilke, Dresler and others. The two authors first named have shown that kephir is of very good service, in quantities of about a litre a day, in gastric troubles such as cardialgia, catarrh, atony, dilatation, vomiting, digestive disturbances and gastric ulcer. The value of kephir in these conditions was recognized at the time of its first introduction into therapeutics, about thirty years ago, and Hallion and Carrion, who have carefully studied kephir, say that kephir milk exerts a beneficial influence on the digestive organs throughout the time it is in them, and, more than that, the influence continues subsequently and is still felt after the use of kephir has been given up. They observed that in the case of hypopeptic subjects the hydrochloric acid in the stomach increased during the kephir treatment, while the urine contained more chlorides. The production of the organic chlorine compounds becomes more normal, i. e., is increased if reduced by the disease, and diminished if increased by the disease, and the acid fermentation in the stomach ceases. In addition we have an improved state of nutrition due to the easy assimilability of kephir, which is far superior to that of milk, and to the properties already described which are due to the micro-organisms of kephir milk. In gastric troubles we cannot, as a matter of course, use kephir in as large an amount as appears necessary in tuberculosis. Individual adjustment of the dosage is advisable. Hallion commences with the same dose in all cases, viz., 1 to 2 glasses a day until the patients have become habituated to the drink. He then increases the amount up to 3 and 4 litres a day. The largest single dose used by him is 200 c. c., for larger doses may cause unpleasant

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Hallion-Carrion, *Therapeutische Monatshefte* 1901, p. 539.

Theodoroff, l. c.

Mandrowski, *Deutsche medizinische Wochenschrift* 1884, p. 324.

Hirsch, *Therapeutische Monatshefte* 1905, p. 71.

Hayem, *Presse médicale* 1904, p. 617.

Löbel, *Medizinische Klinik* 1906, p. 493.

Wilke, *Allgemeine medizinische Zentralzeitung* 1907, p. 239 and 255.

Dresler, *Medizinische Klinik* 1908, No. 27.



eructation. If desired kephir milk may be sweetened by the addition of a little cane sugar. Hallion is opposed as a rule to the warming of kephir before use, and in any case it should not be warmed above 40° C. lest the physical properties of the casein be altered. Hayem has obtained excellent results with kephir treatment in a number of gastric affections. In his experience kephir is specially indicated in gastric troubles accompanied by hyperpepsia, apepsia, feeble secretion and too rapid emptying after meals. Cases with severe diarrhoea are particularly well suited for kephir treatment. Even in cases with apepsia or hyperpepsia due to taking irritants, where inflammatory complications have set in, these are quickly relieved by taking kephir. If the apepsia or hyperpepsia is associated with a delay in the emptying of the stomach due to enfeebled or atrophic gastric muscles, the quantity of kephir taken must be accurately regulated, and we must avoid overburdening with kephir or with other foods. Kephir is also found of value in hyperpepsia with deficient secretion and rapid emptying of the stomach due in most cases to complex changes in the gastric mucous membrane or to parenchymatous, atrophic gastritis, and also in carcinoma of the stomach without demonstrable stenosis. Kephir milk is contra-indicated in hyperpepsia with retarded emptying of the stomach and with excessive secretion, as well as in pyloric stenosis. In general, it should not be used in gastric ulcer, though in chronic cases with slight secretion it may be of great value.

The administration of kephir without other food is preferred by Hayem in apepsia and hyperpepsia with severe diarrhoea, in gastric carcinoma associated with vomiting, and in hyperpeptic consumptive patients with severe diarrhoea. In cases of this kind 5 to 6 glasses are given daily, and the quantity of kephir is increased gradually up to 12 glasses until the time comes for the patient to take a mixed diet, that is to say kephir with other food. In making use of this treatment the long known fact must be taken into consideration that kephir taken when one day old has a slight aperient action, while if taken 3 days old it is somewhat constipating, and when 2 days old its action is almost neutral. Hayem found kephir to have a regulating action both in constipation and in diarrhoea.

In addition to its use in pulmonary tuberculosis and gastric diseases the use of kephir has been recommended in the treatment of anæmia, chlorosis, pernicious anæmia, scrofula, cachexia, chronic bronchial catarrh, kidney diseases (Bright's disease), uric acid diathesis, renal and biliary calculi, chronic rheumatism, chronic infections, in tardy convalescence from debilitating diseases such as influenza, typhoid fever, malaria, etc., in diabetes mellitus, dysentery, chronic intestinal catarrh, habitual constipation, hæmorrhoids, skin diseases (acne, psoriasis, intertrigo, chronic eczema and urticaria), neurasthenia, chorea, hysteria, loss of blood after operations, and general debility.

A point of special interest in connection with kephir treatment is the possibility of adding various drugs to kephir during or after its preparation, and thus rendering it better suited for its particular purpose. Gebhardt has shown that in anæmia the addition of about 0.1 p.c. of lactate of iron to kephir is to be recommended. More recently kephir has been mixed with various other preparations, the use of which appeared indicated in the disease under treatment, including arsenic, the alkaline iodides, creosote, creosotal, guaiacol or guaiacol carbonate\*). These substances should be added before or after the fermentation, according to whether the particular preparation prevents fermentation or not. Thus guaiacol is best added to the finished kephir, while iron preparations, arsenic and iodides may be added when the ingredients of the kephir are first mixed together. Recently R. Kobert has made some valuable contributions on the art of preparing kephir. He showed that in the case of patients who are to exist upon kephir, various nutritive and medicinal substances may be added before the kephir has fermented. Patients with a tendency to constipation are given 10 to 20 grammes ( $\frac{1}{3}$ — $\frac{2}{3}$  oz) of meat somatose in a litre of kephir, and the mixture is taken on the second day. When there is a tendency to diarrhœa skimmed milk is used, and 20 grammes ( $\frac{2}{3}$  oz) of finely ground plasmon are added to one litre. In anæmic patients the addition of 10 to 20 grammes ( $\frac{1}{3}$ — $\frac{2}{3}$  oz) of hæmogallol to a litre of milk is recommended; this is

\*) See Langer, Wiener medizinische Presse 1896, p. 477.

Kobert, Zeitschrift für Krankenpflege 1904, No. 10, p. 377.

Die medizinische Woche 1904, No. 27, p. 219.

a powerful aid to blood formation. The taste of kephir is not altered by this addition.

Kephir milk is not only of use for adults, it is a food possessing excellent properties for children and even for infants, and this fact is becoming increasingly known. In connection with its use in children's practice we have the publications of Monti, Ponomaroff, Olchanetzki, Roxirosa, Dresler and Tollens. Olchanetzki, in using it in the course of his investigations, found that in several respects kephir resembles mother's milk more closely than cow's milk, and therefore considers kephir to be the most suitable substitute for mother's milk. Monti found that children usually objected to kephir at first, or took it unwillingly, but they very soon acquired a taste for it and then asked for it. It agrees with them very well. The action of kephir milk is apparent in an increase of appetite, and of diuresis, coupled with more frequent motions and a rise in weight. Monti prescribed kephir in suitable quantities for infants of 6 months taking account of the fact, already known by that time, that kephir one day old has a slight aperient action, while kephir 3 days old is slightly constipating. When feeding children on kephir exclusively he gave 0.5 to 1 litre a day. It is very exceptional to find that this mode of feeding is not tolerated, and in such cases he found it advisable to interrupt the use of the remedy for a time. In older children Monti considers kephir to be indicated particularly in anæmia, wasting after debilitating diseases, chronic gastric and intestinal catarrh, chronic pneumonia, kidney diseases and articular rheumatism. Excellent results following the use of kephir in children are reported by Roxirosa from the Children's Hospital of Barcelona. It gave specially good results in tuberculosis and rickets. The other authors mentioned above also obtained very satisfactory results from the use of kephir, so much so that Dresler regards the use of kephir

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Monti, Wiener medizinische Zeitung 1887, No. 22 and 23.

Ponomaroff, Archiv für Kinderheilkunde Vol. 5.

Olchanetzki, Dissertation Würzburg 1890, Deutsche medizinische Wochenschrift 1890, p. 589.

Roxirosa, La Medicina de los niños 1905, No. 7.

Dresler, Medizinische Klinik 1908, No. 27.

Tollens, Münchener medizinische Wochenschrift 1908, No. 45.



as an important means toward diminishing infant mortality. This opinion may be somewhat too optimistic, but at any rate the author's results with kephir milk show it to be not only an excellent food for infants, even immediately after birth, but also an excellent remedy in all disturbances of nutrition occurring in infancy.

A. Hirsch was extremely satisfied with the results he obtained from the use of kephir in whooping-cough. Given at the beginning of the disease he found it to have a very favourable effect on the course of the illness. No signs of severe dropsy, considerable hypostasis, marked cyanosis, inflammation of the lungs or eclamptic seizures during the attacks followed the administration of kephir. He prescribed other drugs as well as kephir, so that he was not able to state for certain whether the course of an attack of pertussis was shortened by the action of kephir. He regards the value of kephir in whooping-cough to be due to its diuretic action, which is more powerful than that of milk. He regards it as probable also that in the organism the activity of the bacteria of whooping-cough is inhibited by kephir, or that they are destroyed by it. A further important factor in the action of kephir is its narcotic power. In all severe cases of whooping-cough, after giving kephir for three days, he observed that the children became calmer, and were able to sleep, although they had been deprived of sleep for a long time. This is considered by him to be due to the relief of the passive hyperæmia in the central nervous system, this relief occurring after the circulation has been regulated by kephir. In infants doses of  $\frac{1}{4}$ — $\frac{1}{3}$  litre may be given daily in small cupfuls. If cold kephir is found to have an irritant action it may be warmed slightly before use by placing the cup in hot water. It may also be sweetened by the addition of sugar if its sour taste is objected to.

Kephir is also very useful, in Hirsch's opinion, in scarlet fever and in scarlatinal nephritis. In the initial stages of scarlet fever it diminishes the thirst and maintains the condition of nutrition, while in scarlatinal nephritis it is better than milk treatment. It diminishes the albumin in the urine considerably, so that in 2 to  $2\frac{1}{2}$  weeks, on an average,

the albumin completely disappears. In scarlet fever kephir 3 days old is also preferable, the small amount of alcohol it contains does no harm.

The preparation of kephir is simple enough, although one occasionally comes across very complicated directions for making it. These complicated methods have no advantage over the simpler ones, except possibly in the preparation of kephir on a large scale. The most important point to be considered in obtaining the necessary ingredients is the quality of the kephir (the kephir grains) and of the milk. It is best to use good kephir grains, such as can now be purchased, free from any mouldy or unpleasant smell, for the smell is usually transferred to the kephir milk and spoils its taste. By purchasing kephir the risk of obtaining a substitution product made from ordinary beer yeast and lactic acid bacteria is avoided. For this reason kephir tablets should not be used unless they come from a trustworthy source\*). The milk should only be obtained from cows that are known to be healthy and free from tuberculosis, for in this case there is no need to boil the milk before allowing it to ferment. The question whether boiled or fresh milk is best for the preparation of kephir appears to me to be still in doubt. The Caucasians, at any rate, did not use boiled milk, and there is no reason why such should be preferred provided the milk be hygienically pure, while there is not the slightest doubt that unboiled milk gives the most agreeable kephir. Certainly Forster has said that in kephir fermentation all pathogenic bacteria, such as typhoid and tubercle bacilli, are destroyed. In Broers' opinion, however, this is only true for typhoid, but not for tubercle bacilli. If we are not certain that the milk used is free from tubercle bacilli, it is certainly

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\*) See Hecker, *Therapeutische Monatshefte* 1903, p. 622. — Kephir in tablets is not suitable for the preparation of kephir milk, for Freudenreich has shown that kephir yeast and the *Bacillus Caucasicus* lose most of their vitality when dried. These tablets impart an acid reaction to the milk, which is apt to deceive the uninitiated, but the product obtained by their use does not correspond to a properly prepared kephir milk from good kephir.

Forster, *Allgemeine medizinische Zentralzeitung* 1907, p. 255, *Therapeutische Monatshefte* 1903, p. 625.

Broers, *Tijdschrift voor Geneeskunde* 1906, No. 25.

advisable to boil it. In other cases unboiled milk is preferable, for it is more digestible, while, as a rule, it undergoes fermentation more readily. B. Niederstadt has suggested that the milk should be sterilized before the preparation of kephir, for in his view unboiled milk is apt to serve as a nutrient medium for other noxious fungi, while sterilization increases the peptonizing property of the kephir ferment, and favours the formation of hemi-albumoses. As far as I know, however, neither he nor anyone else has proved this. It is also doubtful whether the danger of infection through tuberculous milk is a very real one, for Möllers showed, a short time ago, that even in infants infection from the milk of tuberculous cows is very rare, and this contingency cannot be compared with the danger of infection from man to man. Whether skimmed milk or full-cream milk should be used depends upon the purpose to which the kephir is to be put. Thus in the presence of diarrhoea skimmed milk should be used, while in constipation full-cream milk is, as a rule, to be preferred. If we merely wish to prepare a refreshing drink, skimmed milk will answer the purpose.

For home use the following mode of preparation is recommended:

5 to 10 grammes (75—150 grains) of kephir grains are introduced into a bottle of 375 grammes ( $12\frac{1}{2}$  oz) capacity, provided with a patent stopper. About 100 c. c. ( $3\frac{1}{3}$  oz) of fresh water are poured over them and they are left overnight. At 8 o'clock the following morning the water is poured away as completely as possible, and the bottle is filled three-quarters full with unboiled milk. The bottle is then left for the day at about  $20^{\circ}\text{C.}$ , well corked, occasionally shaking it gently. In doing this it is best to give the bottle a rotatory movement, for by this the carbonic acid formed is most completely absorbed by the fluid, while the casein assumes a finely divided form. The kephir may be taken at night after straining off the ferment. The ferment is put back into the bottle, and is washed with water, when the bottle is again filled three-quarters full with fresh milk. This kephir may be taken if required as early as the



following morning. The ferment is used again and again for the preparation of new kephir milk until its fermentative action is found to be diminishing. A little new kephir ferment is then added. Kephir will not ripen in a shorter time than that stated. It may be left longer, however, for as long as three days, and it may be left for 5 days provided the temperature be kept below  $20^{\circ}\text{C}$ . The temperature should never be allowed to fall below  $15^{\circ}\text{C}$ . nor is it advisable to allow the temperature to rise above  $25^{\circ}\text{C}$ . during the fermentation of kephir. As a rule 5 days is the longest time that should be allowed, for the later changes which occur in kephir exposed to prolonged fermentation or storage are not definitely known. If a bottle is left to ferment for 3 days in the manner described above, this bottleful may be used at once for the preparation of more kephir. Thus the total amount may be divided among 5 to 10 other bottles, each of these filled three-quarters full with milk, and allowed to ferment for 1 to 3 days, imparting to the bottles occasionally a rotatory movement. Before consumption the ferment may be collected in a suitable sieve, and after washing with water another bottle of kephir milk may be prepared from it. After a time it will be necessary to provide a substitute for the ferment that has reached the stomach of the patient. Theoretically the ferment should be good for an unlimited time, for it is continually regenerated by the fermentation. In practice, however, it is found that the power of the ferment frequently diminishes after a time. This is scarcely due to the fact that some of the ferment is taken with the kephir milk, but is probably a consequence of biological processes. Possibly conditions are apt to arise in which the formation of one or other of the micro-organisms becomes so excessive that symbiosis is upset, so that the normal product of fermentation is no longer evolved. This is apparent by the loss of the pleasant, refreshingly acid taste possessed by a well prepared kephir milk. The weakening of the kephir ferment is said to be evident by the fact that the swollen

\*) Kobert considers a fall of activity due, not to ageing or weakening of the kephir ferment, but to the continual formation of acid. To give it renewed power of fermentation it is merely necessary to wash it with weak solutions of sodium carbonate or bicarbonate.

masses no longer sink to the bottom but float on the surface of the milk. This statement, however, is erroneous.

To prepare kephir in large quantities for sale, the directions given by Kobert are to be recommended:

1 litre of water of 30 to 35° C. is poured over 50 grammes of dried kephir grains. After half an hour this is poured off and is replaced by a like quantity of water of 20° C. After standing for 24 hours the grains which have become whitish are collected on a cloth and are added to half a litre of milk warm from the cow, or of milk that has been warmed. They are left in the milk for 24 hours at ordinary temperature, frequently stirring. The milk is then poured off, the grains are washed well with water, when another  $\frac{1}{2}$  litre of milk is added and is poured off in like manner after 24 hours. These operations are continued for 3 to 7 days until it is found that the fungi, instead of remaining at the bottom of the vessel as at first, begin to rise to the top; at the same time they lose the unpleasant cheesy odour and become yellowish again, but now the fungi require to be fortified by treatment with milk for 5 days before they can be used for technical purposes.

To prepare kephir for use as a beverage, 2 to 3 litres of fresh milk are poured over 250 c.c. of the softened fungus mass, prepared as directed above. This is allowed to stand for 12 to 24 hours at ordinary temperature when the mixture assumes the appearance of cream, and has a pleasant, somewhat acid odour. It is now poured through muslin, if desired the drugs previously mentioned are added, when it is placed in bottles with patent stoppers; the residue left upon the muslin is immediately added to milk to convert the milk into kephir. The bottles are left at ordinary temperature and are shaken from time to time. It is ready for use when it has assumed a fine, flaky consistency. Before use it is thoroughly cooled and shaken.

Of course slight modifications of this method may be made. The kephir drinker learns to adopt such modifications as will suit his taste, and he will soon learn by practice and experience the proper proportions and the best time for starting the fermentation to yield the kephir in the most palatable form. The preparation of kephir is

best carried out in a place in which as far as possible a uniform temperature of about 20° C. is maintained. Fermenting kephir should never be placed in the direct sunshine.

For children, kephir is, as rule, prepared in the way described above. Special directions have been given by Ponomaroff, Dresler and Tollens:

1. Ponomaroff's method. 320 c.c. of full-cream milk are mixed with 1 litre of water,  $\frac{1}{2}$  teaspoonful of sugar and 1 teaspoonful of milk sugar, the mixture is left for 24 hours at 15 to 17° R. (20 to 21° C.) to ferment, with about 10 grammes of kephir ferment, in a well corked champagne bottle. Every hour it is shaken. At the end of 24 hours the drink is ready for use. On the second day of the fermentation, according to the author, the fluid will be found to be frothy and white, and free from casein flakes. It is said to have a sweetish-acid taste, and it is liable to cause eructation. This kephir has been used by Ponomaroff in infants suffering from congenital syphilis, in addition to the usual antisyphilitic treatment, and the more kephir is given the quicker do the dyspeptic symptoms disappear. At the same time the appearance of the stools becomes more normal, the children become quieter, and their condition improves.

2. Dresler's method. A tablespoonful of kephir grains is washed for a short time in very dilute lukewarm soda solution. They are then allowed to swell for 4 to 6 hours in boiled, lukewarm water. A quarter of a litre of previously boiled, cold milk is then poured over them, and this is changed three times at intervals of 12 hours, when the glass, covered with clean filter paper and protected from direct light, is left at a temperature of 14 to 15° R. (17.5 to 18.7 C.). During this time the milk with the kephir grains is carefully shaken 2 to 3 times. Every time the milk is changed the grains are washed with water on a clean sieve. The last portion of milk is left on the kephir grains until it has coagulated and has a uniform firm consistency, which usually occurs within 24 hours. The milk thus obtained is capable of ready fermentation, and may be used for the further preparation of kephir in bottles. Bottles with a capacity of 1 litre are well cleaned, sufficient of this prepared milk is introduced to form a layer about one inch deep, boiled, cold



milk is added to make the bottle three-quarters full. The bottles are well shaken and left for 24 hours at 14 to 15° R. (protected from light). During this time they are gently shaken twice. The kephir milk is now ready for use and is kept in a cool place until required (12 to 13° R.) to prevent further fermentation. A small quantity of the finished kephir milk is left in the bottles and is allowed to stand for 12 hours longer. The bottle may then be filled again with milk and a second bottleful of kephir milk may be prepared. Kephir one day old should not, in Dresler's opinion, be used for the preparation of new kephir milk, as otherwise the product will have a musty smell and taste. Dresler is emphatically in favour of using boiled milk since experiments carried out at the Kiel Hygienic Institute failed to confirm Forster's statements (see above). It should be added that Dresler now directs that the bottles should not be tightly closed if large quantities are to be prepared, for it would be cumbersome if the bottles required to be frequently shaken individually. If the bottles are placed in a room free from dust, or merely covered with paper he found that they could be left to themselves and would yield a perfect kephir by the following morning. The quantity required for a litre of kephir was about 125 grammes of 2 days old kephir.

Dresler prepared his kephir in accordance with the above directions, either with boiled water or with thin rice mucilage to suit the age and the condition of the digestive organs, for administration to children of 7 or 8 months; older children are able to take it undiluted. To make it easier for children to grow accustomed to kephir, the author added 1 saccharine tablet to each bottle of kephir. Other additions, such as Soxhlet's nutritive sugar, have been made by Dresler when he has thought they would be useful. On the whole Dresler's experience proved that kephir is not merely an auxiliary therapeutic agent, but actually a first-rate nutritive substance. He has obtained excellent results when it has been the sole form of nourishment given immediately after birth, and when it has been given to infants in conjunction with other nutritive substances, in disturbances of nutrition and in gastro-intestinal diseases from

the slightest to the most severe forms. Klotz made a study of yoghourt which he considered to be preferable to kephir for children, because it contains less alcohol; Dresler, in a more recent communication, points out that the small quantity of alcohol contained in kephir prepared according to his directions is quite harmless, and never produces the slightest unwelcome effect. Thus he had an opportunity, in the families of two colleagues, to carry out kephir treatment for their babies, although at first they objected to its use on account of the alcohol it contained. Both colleagues admitted, after months of feeding on nothing but kephir, that they had failed to detect the slightest action due to the alcohol it contained, in spite of careful observation, while the bodily and mental development had to their great joy been excellent. He mentions this to set aside the doubts of those colleagues who are particularly careful, or who are abstainers, with regard to the effects of the alcohol present in this preparation. As for yoghourt, he does not consider its use advisable as a food for infants, because it contains considerably more acid than kephir milk. In his experience, moreover, there are infants who are sensitive to sour milk preparations. This intolerance may be found in almost all infants when digestive or gastro-intestinal disturbances are present. For this reason kephir milk, which contains but little acid, is decidedly preferable to yoghourt. Sensitiveness to acid may occur with the use of kephir, and in such cases the author advises the use of lime water which he regards as the best means of habituating patients to sour milk. In his own words: "My first trials with kephir convinced me that kephir was less readily tolerated by children in severe illness the more acid it contained. The most varied percentages of acid may be obtained in kephir by taking a larger quantity than usual and allowing it to mature at a temperature higher than the optimum, shaking it several times a day. The presence of 10 p. c. of acid was badly tolerated, while when it contained 12 p. c. it could not be used for children who were severely ill. It is therefore a matter of fundamental importance in the use of sour

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Klotz, Zeitschrift für diätetische und physikalische Therapie, Vol. 12, No. 5.

Dresler, Medizinische Klinik 1910, p. 1214.

milk preparations to use only such as contain less than 10 p. c. of acid\*). For this reason I have made no trials with yoghurt in children, although it has been over-valued and extensively advocated, for it contains so much acid (15 p. c.) that I was justified in assuming that the results would be uniformly unfavourable. Another point of fundamental importance in the use of sour milk is to avoid the addition of sugar or of a solution of sugar until convalescence is well established and the stools have been alkaline for a considerable time".

3. Tollen's method. A stock solution is first prepared with kephir by allowing the ferment to act upon milk for 48 hours. The kephir milk thus obtained is diluted with 4 times the quantity of fresh milk, and the mixture is again allowed to ferment for 48 hours. If the kephir has a musty smell or taste, this is removed (so Tollens states) if this manipulation is repeated several times. The kephir milk thus obtained is used as a stock solution, one part of it being mixed with 4 parts of milk, and allowed to ferment in well stoppered bottles. Fermentation is started by the kephir organisms present in the stock solution. If the fermentation is started at mid-day, and the bottle is shaken several times in the course of the afternoon, it may be used the following morning. Tollens states that exposed to a temperature of 16 to 18° C. kephir requires about 18 hours to mature. If we use only  $\frac{4}{5}$  of the finished kephir milk, and make up the rest with fresh milk, this will also be ready for use after 18 hours. If litre bottles are used all the kephir milk, except  $\frac{1}{5}$ , may be poured off, and what remains is just the right amount for an infant's consumption for a single day. It is diluted with a 6 p. c. sugar solution and given in six portions. As soon as the age and weight of the child have advanced sufficiently to necessitate less dilution than the addition of one-third of sugar solution to provide sufficient nourishment, it is best to change to pure milk feeding, for concentrated kephir is apt to cause diarrhœa.

For the sake of completeness I would point out that attempts have been made to use a solution of sugar instead

\*) The author speaks of % (percentages) in the original paper. This is probably either a technical expression or a misprint, for kephir may contain 1 to 1.5% of acid, but not 10—15%.



of milk in the preparation of kephir. It is clear from the account given above of milk kephir that little result was to be expected from this attempt. The so-called "water kephir" has absolutely no nutritive value. J. Carteret ascribes the principal value of "kéfir à l'eau sucrée" to its refreshing properties. His method of preparation is as follows: 100 grammes of powdered cane sugar are dissolved in 2 litres of water, and stirred up with 1 litre of kephir grains, when the mixture is left in a covered vessel at a moderate temperature for 3 days. The fluid is then transferred to champagne bottles which are well corked and left for 2 or 3 days in a cool place (at about 15° C.). A yellowish fluid is thus obtained, which is said to taste like cider. Carteret states that water kephir has the following composition: 0.14 p. c. alcohol, 0.1 p. c. acid, 0.21 p. c. carbonic acid, 0.25 p. c. extract, 1.6 p. c. sugar, and 0.05 p. c. salts. So large a quantity of kephir is certainly not needed, for the cost of the drink becomes excessive. It is very probable, however, that Carteret's suggestion has received no attention, for no further references to water kephir appear in the literature.

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Carteret, *Presse médicale* 1899, No. 2, p. 5.

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## Preparations and Drugs.

### Acetone.

The treatment of uterine carcinoma by acetone was introduced some time ago by Gellhorn. An interesting paper has been contributed by Richter dealing principally with the results of fulguration in inoperable cancer of the uterus. The author found it useful to combine fulguration with acetone treatment, the vagina being first swabbed out, and crude acetone being poured into the vagina through a milk-glass speculum in sufficiently large quantity to half fill the speculum. This is repeated 2 to 4 times a month. The acetone is left in the vagina for 10 minutes or even longer. After its removal the vagina is swabbed out, and a glycerin tampon is inserted. Richter found that the drug hardens the tissues to such an extent as to considerably diminish hæmorrhage. It also diminishes the fœtor by preventing disintegration, while it acts as a powerful deodorant. The author obtained excellent results in the case of a patient in whom an attempt at total extirpation per vaginam had to be abandoned because the carcinoma was found to be too far advanced. The patient was treated solely with acetone which was applied some 80 times, in the manner described above. The author reports on the condition of the patient more than 20 months after the first acetone treatment. The vagina is almost stenosed, the finger cannot be inserted further than  $2\frac{1}{2}$  cm. (1 in.), and it meets with firm taunt scar tissue in all directions. The favourable action of acetone was made use of by Richter in other cases, although the results were not uniform in the case of tumours of different degrees of malignity.

### Acidum aceticum.

Acetic acid has often been recommended, either in its pure concentrated state or diluted, for the detection of protein substances in physiological fluids, the same as it

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Gellhorn, Merck's Reports 1907, p. 1. — Journal of the American Medical Association 1907, No. 17.

Richter, Münchener medizinische Wochenschrift 1910, No. 17, p. 891.

is largely used for the demonstration of albumin in urine. It has been recommended by Moritz and Rivalta for distinguishing transudates from exudates. Moritz found that the addition of acetic acid (5 p.c.) produced a turbidity in the case of exudates, while in transudates no reaction was obtained. Rivalta modified this reaction by dropping the fluid that was to be tested into dilute acetic acid. The results and the value of this reaction have been variously commented upon by different investigators, and K. Pieper has recently gone into the question. He found that the acetic acid test performed with various puncture fluids, whether the test were applied in Moritz' or in Rivalta's way, was a very useful one for distinguishing between transudates and exudates. All exudates tested gave a turbidity with dilute acetic acid, while all transudates remained clear. It is easier to judge whether we are dealing with a transudate or an exudate in the case of pleural fluid than in the case of ascitic fluid.

Rivalta's test will not serve to distinguish normal from pathological cerebro-spinal fluid, but Moritz' test is a useful and trustworthy one for this purpose. Pieper declares that the fluid from a lumbar puncture is to be regarded as having been modified by acute inflammation if the addition of a few drops of acetic acid (5 p.c.) produces a definite turbidity visible by transmitted light or when held against a dark background. In general the author therefore prefers Moritz' test. He gives the following directions:

About 2 c.c. of puncture fluid are taken, and 1 to 2 drops of acetic acid (5 p.c.) are added from a drop bottle. In the case of an exudate a definite, more or less dense turbidity occurs, which frequently increases to a flaky precipitate, while in the case of a transudate this opacity does not appear, or else it appears on the addition of more acetic acid, usually 4 to 5 drops, and then takes the form of a slight opalescence when viewed by reflected light, or an almost transparent opacity by transmitted light. In the case of an exudate the behaviour with the first drop of acetic acid is frequently characteristic, for it leaves a well

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Moritz, Dissertation 1886.

Rivalta, Berliner klinische Wochenschrift 1908, No. 12, p. 630.

Pieper, Münchener medizinische Wochenschrift 1910, No. 1, p. 11.



marked milky-white turbidity which disappears on shaking. The second drop then causes a permanent turbidity.

### **Acidum boricum.**

In lymphatic scrofulous affections of the eye, J. Eisenstein suggests that finely powdered boric acid may be used with advantage instead of calomel. In eczematous affections of the conjunctiva and cornea it is said to be a very good remedy in all stages of the disease. The author gives the following directions for its use: The eyelids are everted, and this can frequently be done in the case of photophobic patients by energetically separating the margins of the lids with the thumb and forefinger of the left hand. The powdered boric acid is then applied in a fairly thick layer by means of a brush upon the posterior surface of the lids. The lids are released, when they fall back at once upon the eyeball and the powder is then spread by means of the thumb of the right hand placed upon the upper lid. In some cases this may be done more or less energetically, though in the case of deeper seated ulceration it must be done with care. This procedure inflames the eye and should be followed by the instillation of a drop of cocaine solution (1 p. c.), whereupon the pain leaves off in a few minutes. Of course in severe cases, especially in corneal ulcers, the author uses atropine, dionin, pilocarpine, eserine, and protective bandages and compresses, galvano-cautery, peritomy, etc., in accordance with the recognised practice in ophthalmology, although he regards boric acid as the essential specific agent in the local treatment of these diseases of the eye. He continues its use as long as inflammation is present, after which, provided only cicatricial opacities remain, he uses massage and Pagenstecher's ointment. The author considers boric acid an important remedy in trachoma in lymphatic persons. Boric acid insufflations are first made to eliminate that part of the inflammation which is due to the lymphatism. The actual granular ophthalmia then becomes more clearly differentiated and is far more readily dealt with by suitable methods.

**Acidum hydrochloricum.**

Beebe and Rüdisch have observed that in pernicious anæmia there is frequently a deficiency of hydrochloric acid. They accordingly felt justified in treating this disease with large doses of hydrochloric acid. Beebe prescribes a mixture containing 150 drops of hydrochloric acid in 300 c. c. (10 oz) of water. 120 to 360 c. c. (4—12 oz) are given half to one hour after each meal. He found that in cases in which this treatment led to improvement the patient's condition relapsed when the administration of hydrochloric acid was left off. If the improvement were so far advanced that there was a demonstrable increase in the hæmoglobin in the blood, the treatment could be left off without fear of a relapse. The author states that on the whole his results were satisfactory. Rüdisch reports one case of the treatment of pernicious anæmia which is in agreement with this statement. In this case there was a deficiency of hydrochloric acid, and the author gave pepsin and hydrochloric acid, using 105 drops of dilute hydrochloric acid 3 times a day (15 drops in iced water every 10 minutes). Under this treatment he found that the number of erythrocytes rose from 1,800,000 to 3,250,000, while the leucocyte count diminished by about 50 p. c. and the hæmoglobin content was doubled. The abnormal bodies characteristic of the disease disappeared from the blood, and the patient gained considerably in weight.

Following Falkenstein, Solger obtained surprisingly good results with hydrochloric acid in the treatment of gout. He himself had suffered for 12 years from uratic arthritis, and the attacks had increased in frequency and in severity as time went on. He adopted Falkenstein's suggestion, and took increasing doses up to 60 drops of hydrochloric acid in water, with the result that a rapid change for the better was produced. By way of secondary effects diarrhoea occurred at the beginning of the hydrochloric acid treatment, but this left off before long without special treatment. The author has remained free from attacks of gout for more than a year, and in the absence of other measures

Beebe-Rüdisch, *Klinisch-therapeutische Wochenschrift* 1910, No. 18, p. 453.

Falkenstein, *Merck's Reports* 1904, p. 7.

Solger, *Deutsche medizinische Wochenschrift* 1910, No. 33, p. 1546.

or alteration in his mode of living he attributes his immunity solely to the action of the hydrochloric acid.

### **Acidum lacticum.**

The physiological processes in the vagina, as explained some time ago by Döderlein, showed that the bacteria normally present in the vagina and their products afford protection from infection by pathological bacteria. Normally the vaginal secretion is strongly acid owing to the products of the bacteria present, and for this reason infection cannot take place. Pathological vaginal secretion, however, is but slightly acid, or is neutral, hence foreign germs are readily able to grow in it. The acid reaction of the normal vaginal secretion is due to the presence of lactic acid which is formed by the vaginal bacteria. The amount of lactic acid present in normal vaginal secretion was given by Döderlein as 0.945 p. c., while Zweifel established that it was present in the form of fermentation lactic acid ( $\alpha$ -oxypropionic acid or inactive ethylidene lactic acid  $\text{CH}_3 \cdot \text{CH}(\text{OH}) \cdot \text{COOH}$ ). These authors were led by their practical experiments to recommend the use of a 0.3 to 0.5 p. c. solution of lactic acid for the prophylactic and curative treatment of the vagina, but this suggestion appears to have found little support. N. Cukor considers the great value of the artificial introduction of lactic acid to depend on its replacing and increasing the normal lactic acid content of the vagina, thus rendering the vagina unsuitable for the growth of pathogenic bacteria. In his opinion the reason it is so little used is due to the high price of lactic acid. If we consider that the solutions required are as weak as 0.3 to 0.5 p. c. a glance at the (German) official medicine tariff will show us that this is not the case. It should be remarked that recently 15 and 50 p. c. lactic acid has been placed on the market under the name of "Laktolavol".

Communications by R. Kaiser show that lactic acid is useful in the local treatment of tuberculous troubles,

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Döderlein, Deutsche medizinische Wochenschrift 1895, p. 157.

Zweifel, Archiv für Gynäkologie 1908, Vol. 86.

Cukor, Klinisch-therapeutische Wochenschrift 1909, p. 1332.

Kaiser, Dissertation, Freiburg 1909. — Allgemeine medizinische Zentralzeitung 1910, No. 18, p. 244.



especially in the treatment of conjunctival and scleral tuberculosis. It is particularly well suited for this purpose, its action being almost specific, while it has very little irritant action.

E. Stanton Faust has investigated the pharmacological action of lactic acid, to ascertain whether lactic acid can be used in the place of other acids, such as tartaric and citric acid, in food stuffs. He found this to be the case, provided the food does not contain more than 5 p. c. of lactic acid. He therefore gives 5 p. c. as the highest limit of lactic acid to be permitted even though the organism is able to consume higher concentrations. Further, it has less irritant action than acetic acid, and has the advantage over tartaric and citric acid of possessing antiseptic and bactericidal properties. The sodium lactate formed in the bowel has an aperient action and may hence be useful in aiding evacuation of the large intestine and the removal of noxious products of decomposition. It follows from this that the use of lactic acid in food in the concentration mentioned is not accompanied with any danger.

#### **Acidum nucleinicum.**

In a remarkable paper on the value of nucleinic acid in the treatment of progressive paralysis, J. Donath states that the action of injections of nucleinic acid, sodium nucleinate, or of tuberculin appears to depend on an increased oxidation paresis. Though the action is similar, nucleinic acid has the advantage of being non-poisonous. In 70 p. c. of the paralytic patients in whom it was used, injections of a 2 p. c. sodium nucleinate solution led to a decided improvement, while in 50 p. c. of the cases the patients were able to return to work. Injections were given at intervals of 5 to 7 days. On an average 8 applications and 8 grammes (120 grains) of sodium nucleinate were required. The following solution was used:

Rp. Sod. nuclein.	2.0 (30 grains)
Sod. chlor.	2.0 (30 grains)
Aq. dest. steril.	100.0 (3 $\frac{1}{3}$ oz)

Stanton Faust, *Chemiker-Zeitung* 1910, p. 57. — *Apotheker-Zeitung* 1910, p. 72.

Donath, *Allgemeine Zeitschrift für Psychiatrie und psychisch-gerichtliche Medizin* 1910, No. 3. — *Psychiatrisch-Neurologische Wochenschrift* 1910, No. 15.

No harmful secondary effects were observed. The above mentioned good results are in contrast to those reported by J. L  pine. Of 17 cases one only reacted to nucleinic acid injections by a slight improvement. In several psychoses, however, L  pine obtained good results with this treatment. The author was led to use it by the consideration that psychoses are sometimes favourably affected by a severe infective disease, so that an appreciable benefit might arise from an artificially produced severe reaction of the organism in which the polynuclear leucocytes were concerned. For this purpose he used injections of sodium nucleinate. He found that it exerted a definite, though variable effect on the psychic condition, which might be regarded as favourable. The results were specially good in acute and subacute mania and in periodic insanity. In dementia pr  cox and degenerative delirium the results were satisfactory, while there was practically no effect in epilepsy, senile dementia, delusions of persecution and morbid fear. The dose generally used by the author was 50 c.c. of a 1 to 5 p.c. solution of sodium nucleinate. From a theoretical point of view the results obtained by L  pine are of interest in showing the connection between psychic disturbance and the biological processes in the organism.

E. von Graff tested nucleinic acid for its effect upon the morbid processes during birth and the puerperium, and came to the conclusion that nucleinic acid was not able to produce a sufficient leucocytosis during the critical days of the puerperium. The prophylactic use of the remedy during childbirth led to an equally negative result.

The communications of L. Mezernitzky are also of interest, as they show that sodium nucleinate has a diuretic action. Doses of 5 to 15 grammes (75—150 grains) are said to have a powerful diuretic effect in cirrhosis of the liver and ascites, causing the rapid disappearance of the ascites.

Injections of nucleinic acid were recommended some years ago by Chantemesse in post-operative peritonitis, and

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L  pine, Lyon medical 1910, No. 9.

Graff, Zentralblatt f  r Gyn  kologie 1910, No. 27.

Mezernitzky, Kongre   f  r innere Medizin, Wiesbaden 1910. —

M  nchener medizinische Wochenschrift 1910, p. 1032.

Chantemesse, Merck's Reports 1907, p. 11.

in hæmorrhage in typhoid fever. The high therapeutic value of this treatment has been recently confirmed in a work by Candela y Pla.

### **Acidum picricum.**

Former communications in these Reports have shown that picric acid is of value in a number of affections of the eyes. It has great keratoplastic power, and appears to be a powerful agent in restoring epithelial and cutaneous tissues. These properties of picric acid are fully confirmed in the reports of E. Fabri and M. Ohlemann. Fabri has tested the statements as to the value of the acid in corneal burns caused by lime, as described years ago by Fortunati. He obtained excellent results. The acid gives very good results, too, in injuries to the cornea and conjunctiva caused by foreign bodies. The author applied it immediately after removal of the foreign body in the form of the ointment recommended by Fortunati:

Rp. Acid. picric. 0.05—0.1—0.15 ( $\frac{3}{4}$ — $1\frac{1}{2}$ — $2\frac{1}{3}$  grains)  
Cocain. hydrochlor. 0.1 —0.2—0.3 ( $1\frac{1}{2}$ —3—5 grains)  
Vasel. Americ. alb. 12.0 (180 grains)

Healing followed within 1 to 2 days without scarring; even severe burns of the cornea extending through two-thirds of the surface were healed. The author gave statistics to prove his results.

The statements of Ohlemann are equally favourable. He found a 2 p. c. picric acid ointment of good effect in various inflammatory affections of the eye, as the acid is too sparingly soluble in water. The only unpleasant by-effect due to picric acid treatment is the yellow colour imparted to the lids. It is said that this can be prevented to some extent by thorough cocainization. After applying the ointment the eye is covered with a protective dressing.

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Candela y Pla, *Cronica medica* 1910, March 10.

Fabri, *Bollettino dell'ospedale oftalmico della provincia di Roma* 1909, July. — *Revue internationale de médecine* 1910, p. 322. — *Wochenschrift für Therapie und Hygiene des Auges* 1910, No. 17, p. 138.

Ohlemann, *Wochenschrift für Therapie und Hygiene des Auges* 1910, No. 13, p. 103.

Fortunati, *Annali di ottalmologia* 1907. — *Semaine médicale* 1907, p. 515. — *Merck's Reports* 1907, p. 16.



In conjunctival catarrh the author used the acid in the form of solutions and ointment, and obtained a diminution in the inflammation and in the secretion in severe cases. In suitable cases the use of picric acid may also be combined with the application of silver nitrate with particularly good results. In diphtheritic and pseudo-diphtheritic inflammation and in gonorrhœal ophthalmia, the acid is said to have no particular action. It is useful, however, in ophthalmia neonatorum when the cornea is ulcerated. In such cases the use of a picric acid ointment is appropriate. It readily checks the necrotic process, while the tissues become transparent within a relatively short time. In pustular conjunctivitis Pagenstecher's ointment is preferable.

Picric acid is of no use in vernal catarrh, though it is of great value in the papillary and granular forms of trachoma, for under its influence the patient is better able to keep the eyes open and to bear the light. It also diminishes the sensation of foreign bodies being present and the lachrymation; in fact it effects relief which justifies its use. Ohlemann knows of no contra-indications, and there are very few cases in which intolerance is observed. The greater the hyperæmia of the bulb and palpebral conjunctiva, the more rapid and certain is the result.

In perforation of the tympanic membrane picric acid has given good results. R. Stevani cleanses the ear by the dry method, and then instils 10 drops of a solution of 1 gramme (15 grains) of the acid in 20 grammes ( $\frac{2}{3}$  oz) of alcohol and 100 grammes ( $3\frac{1}{3}$  oz) of water. The ear is then plugged with sterile gauze, treatment being continued every day until the discharge has left off.

Gazzetti and Sarti used picric acid as a reagent for ammonium sulphide in the urine. An excess of alkali is added to the urine, whereupon picric acid solution is added. In the presence of ammonium sulphide a red colour appears, due probably to the formation of picraminic acid. This colour disappears on the addition of sulphuric acid.

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Stevani, Bollettino delle malattie dell'orechio 1910, No. 5. —  
Progrès médical belge 1910, p. 158.

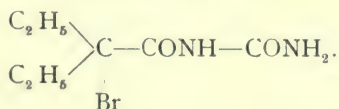
Gazzetti-Sarti, Archivio di Farmacologia sperimentale 1910, p. 319.

**Acidum sulphurosum.**

Sulphurous acid was formerly used in the form of inhalations for the treatment of pulmonary tuberculosis. E. Talini tried its use in the form of intramuscular injections, and states that his results were satisfactory. At first he used a solution of 0.5—5.0 grammes ( $7\frac{1}{2}$ —75 grains) of sodium bisulphite in 100 c. c. ( $3\frac{1}{3}$  oz) of normal saline solution, of which doses of 2—5 c. c. (34—85 min.) were employed. Having ascertained that these injections were well tolerated, he added free sulphurous acid to the injection fluid, 1 p. c. of sulphur dioxide being added to the 5 p. c. solution of bisulphite in normal saline. Adults were given an injection of 5 c. c. (85 min.) daily, children 3 c. c. (50 min.). This mixture is said to act better than the former. To give it tonic properties he applied, in addition to 3 c. c. (50 min.) of this solution, 2 c. c. (34 min.) of a 5 p. c. solution of calcium chloride in normal saline solution. This treatment led to an improvement in the general condition, especially to a gain in weight, while the catarrh diminished and the night sweats and the fever were reduced. As soon as appreciable improvement was obtained the injection was given every other day, and finally twice a week. Even when the injections were continued for a long time the author never observed albuminuria as a consequence of the treatment.

**Adalin.**

Adalin is a derivative of urea, brom-diethyl-acetyl urea, corresponding to the formula:



It is a white, crystalline powder, almost odourless, with a slightly bitter taste. It melts at  $116^\circ\text{C}$ . It is very slightly soluble in water (about 8:10,000 at  $20^\circ\text{C}$ .). It is rather more soluble in hot water and in olive oil.

The exhaustive pharmacological investigations of E. Impens have proved that adalin is a fairly powerful hyp-

notic, and as its absorption takes place slowly, its action is somewhat wanting in uniformity. Its toxicity is moderate, so that it may be used without danger for therapeutic purposes. With regard to the elimination of the new remedy the author found in dogs and rabbits that brom-diethyl-acetyl urea is excreted in three forms simultaneously: as inorganic bromide, as a bromide of a fatty acid and as a bromide of an organic neutral compound, which is soluble in ether.

P. Fleischmann tried the use of adalin principally as a hypnotic, but also as a sedative. As a hypnotic it gave good results in the most varied conditions of insomnia due to over-excitability of the central nervous organs, or to excitement, fear and worry, though he was not able by its use to combat severe pain, cough or dyspnoea. The doses used by Fleischmann for adults were 0.5—1 gramme ( $7\frac{1}{2}$  to 15 grains) and by way of experiment 2 grammes (30 grains) the larger dose prolonging the action without giving rise to the slightest secondary symptoms. The treatment might be prolonged for 10 to 14 days, giving 1 gramme (15 grains) daily, without setting up any cumulative effects. As a hypnotic the remedy gave satisfactory results, but in testing its sedative action in rheumatic chorea, Graves' disease and cardiac neuroses with tachycardia the author obtained no definite effect.

In mental diseases adalin has a marked sedative effect, according to J. Finckh, but the dosage must be suitably adjusted. The author gave as much as 3 grammes (45 grains) a day in 4 or 5 portions. These doses were always well tolerated, though after prolonged use the action appeared to diminish slightly. Moreover the action of the remedy was occasionally wanting in uniformity, and Impens has already drawn attention to this observation. The action of adalin in epilepsy is due, in the author's opinion, to the hypnotic property of the component of adalin which contains no bromine, and not to the bromine component. Since the preparation quickly leaves the organism it would appear scarcely suitable for extensive use in epilepsy, still less as a substitute for bromine preparations. In psychiatrical prac-

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Fleischmann, *Medizinische Klinik* 1910, No. 47, p. 1859.

Finckh, *Medizinische Klinik* 1910, No. 47, p. 1860.



tice Finckh considers that the combination of adalin with other hypnotics, such as chloral hydrate, trional, tincture of opium and especially paraldehyde ought to give good results.

### Adrenalin.

About a year ago W. Falta and L. Ivčovic, as a result of their pharmacological experiments, showed that adrenalin is a powerful antagonist to strychnine, so that it will serve as an antidote to strychnine. Exner some time ago found that adrenalin has the power of delaying the absorption of poisons, and H. Januschke made some experiments to ascertain whether adrenalin might really be considered a specific antidote for strychnine. He was able to demonstrate that adrenalin was not able to prevent strychnine from poisoning the central nervous system in animals; its effect was merely to retard its absorption in the manner Exner had described. Falta and Ivčovic, in making similar experiments, found that the frog's heart which had been caused to stand still in diastole by strychnine, could be made to beat once more by adrenalin, but that this result was due not to a specific antagonism, but to a stimulating action, for other stimulants, mechanical, electrical and chemical (camphor, barium, strophanthin and atropine) produce the same effect.

With regard to the use of adrenalin in asthma we have the communications of B. Melland, P. W. Panfilow and Matthews. Matthews considers that the immediate cessation of an acute attack after spraying the nose (with a solution of 1:4000—1:1000) has not been satisfactorily explained theoretically. He attributes its action in hypertrophic rhinitis to the contraction of the swollen mucous membrane, and to a transitory relief of the peripheral irritability. In a case of bronchial asthma with well-marked dermatographism, Panfilow assumed that theoretically subcutaneous injections of adrenalin should act, and he was able, in fact, to cut short the attack every time by the application of 0.2 c. c.

Falta-Ivčovic, *Berliner klinische Wochenschrift* 1909, p. 1929.

Exner, *Zeitschrift für Heilkunde* 1903, No. 12.

Januschke, *Wiener klinische Wochenschrift* 1910, p. 284.

Melland, *Lancet* 1910, No. 4525, p. 1407.

Panfilow, *Medizinskoe Oboshrenie* 1909, No. 7. — *Fortschritte der Medizin* 1910, p. 980.

Matthews, *British Medical Journal* 1910, No. 2564, p. 441.

(31½ min.) of adrenalin solution (1:1000). Since adrenalin acts as a vaso-constrictor the author regards the success of his method as supporting the theory of the angio-neurotic origin of asthma. Melland applied 5 to 10 drops of adrenalin solution (1:1000) in spasmodic asthma subcutaneously, and was satisfied with the effect produced in every case.

The vaso-constrictor action induced E. N. Thornton to try it in bubonic plague. He hoped to relieve or prevent the general congestive condition, and he appears to have been successful. He began by giving 30 drops of adrenalin solution (1:1000) every 4 hours for 3 days, with 10 drops of tincture of strophanthus. He then continued with 3 doses daily. In severe cases he gave the preparation at the beginning of the treatment, and so long as there was danger he gave it also subcutaneously and intravenously. In bubonic plague 20 drops of adrenalin solution were injected into the tissues in the neighbourhood of the swellings. The effect of the adrenalin treatment was evident in the improvement in the strength of the heart coupled with a rise of blood pressure, while the delirium and sleeplessness were not improved. The mortality was appreciably reduced, and even in the cases which ended fatally it was found that the congestive changes, particularly in the suprarenals, were less extensive, while the plague bacilli were present in smaller numbers in the tissues than in cases that had not been treated with adrenalin.

In serous effusion, pleurisy, peritonitis and ascites adrenalin has been found by Pascucci to have been of good service. The author injected 2 to 8 c.c. (34—136 min.) of adrenalin solution (1:3000) into the serous cavity. He found that the absorption of the effusion was considerably accelerated by the injections. The treatment gave rise to no unpleasant secondary effects.

Kownatzki has reported on the value of adrenalin in osteomalacia. It is well known that Bossi had previously reported excellent results with the use of this remedy in this disease, but his results had not been fully confirmed by more than a few of those who had repeated his experiments. Kownatzki treated an apparently hopeless case of

Thornton, *Lancet* 1910, No. 4519, p. 994.

Pascucci, *Clinica medica italiana* 1909, No. 7.

Kownatzki, *Münchener medizinische Wochenschrift* 1910, p. 1549.

osteomalacia with adrenalin and obtained a cure in a short time, thus proving that there are cases of ostemalacia which are amenable to adrenalin treatment. We are not able at present to distinguish such cases from those which cannot be influenced by it, and the action of adrenalin in osteomalacia is at present entirely beyond our power of calculation.

In veterinary medicine a communication of K. Hutschenreiter is of interest. He found adrenalin injections to prove of good service in nasal hæmorrhage in race horses. The author gave 5 c.c. (85 min.) of the commercial solution (1:1000) subcutaneously, immediately in front of the shoulder, and then caused the animal to be tied up for 24 hours to prevent its worrying the seat of the injection. He gave the animal soft food during this time.

A new reaction for adrenalin is given by A. J. Ewins. A solution of adrenalin is warmed with a 0.1 p.c. solution of potassium persulphate when an intense red colour appears, and may be seen even in solutions with a fairly dark colour. The limit of the sensibility of this reaction is reached with a dilution of one of adrenalin in 5,000,000 of water.

### **Adrenochrom.**

Diesing showed some time ago that Virchow was right in supposing the yellowish-green colouring matter of the substance of the suprarenal to be due to an organic compound of sulphur. He found further that this colouring substance had a powerful action on the animal organism. He therefore tried its use in the treatment of gout. His results were very satisfactory, particularly when used in combination with mud baths and dietetic measures. In 19 cases of arthritis and rheumatism he obtained either a cure or an improvement. He therefore considers this new suprarenal preparation, which he calls "Adrenochrom", to be the best drug for gout, provided the necessary physical treatment be given at the same time. Further trials are necessary to establish which forms of gout are specially amenable to adrenochrom treatment. He recommends its

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Hutschenreiter, Tierärztliches Zentralblatt 1910, No. 8.

Ewins, Journal of Physiology, Vol. 40, p. 316.

Diesing, Medizinische Klinik 1910, No. 13, p. 507. — Zentralblatt für Physiologie und Pathologie des Stoffwechsels 1909, No. 10.



trial more especially in cases in which the salicylic preparations, lithium salts and colchicum have failed. The dose for internal use is 0.025—0.05 gramme ( $\frac{2}{5}$ — $\frac{3}{4}$  grain) of adrenochrom 3 times a day. The preparation may also be administered intramuscularly.

### Æther.

The method of intravenous ether anæsthesia introduced by Burkhardt\*) has aroused widespread interest. The communications of various workers in this field may therefore be briefly considered.

P. Janssen was the first to express hesitation in using the intravenous ether method. In his opinion the anæsthetist who uses it is not constantly aware of the dosage he is using, moreover, the author fears that changes may be produced in the constituents of the blood by the action of the ether saline solution as recommended—changes which might lead to clotting and embolism. These fears are set at rest by Burkhardt who made experiments on animals and men. He pointed out that a solution with not more than 5 p.c. of ether never produced unpleasant secondary symptoms in his experiments. Burkhardt does not suggest that his method should supplant the older inhalation method. He regards it as completing the older method, especially when there are changes in the respiratory organs which render inhalation anæsthesia unduly risky. With regard to the possibility of an over-dose, Burkhardt considers this scarcely likely because the injection fluid contains very little ether (5 p.c.). In any case it is urgently desirable to test the intravenous method of anæsthesia more fully. As far as this has been done by others up to the present, it has received little support, as the following statements show.

Küttner made 23 trials, and regards the intravenous use of ether as not free from danger. He agrees with Janssen in fearing the possibility of embolism, and in two cases, on the day following the anæsthesia, infiltration of the lungs set in. Hence pulmonary complications cannot always be prevented when the new method is used.

\*) See Merck's Reports 1909, p. 69.

Janssen, *Münchener medizinische Wochenschrift* 1910, No. 3, p. 136.

Burkhardt, *Münchener medizinische Wochenschrift* 1910, No. 7, p. 361.

Küttner, *Zentralblatt für Chirurgie* 1910, No. 6 and 7.

Küttner's view is backed by F. M. Pikin, H. Schlimpert, A. Brüning, Clairmont and W. Denk. Schlimpert obtained very bad results in 6 cases. In 1 case only, an exploratory laparotomy, did Burkhardt's injection prove sufficient. Moreover, he observed clotting of blood at the point of introduction of the cannula. For this reason he considers the method unfit for use at present. Brüning disapproves of it on theoretical grounds, Clairmont and Denk by reason of their experiments on animals. Schmitz-Pfeiffer observed the formation of thrombi at the seat of the infusion; he regards this as an objection to the intravenous method. In 38 cases he observed no other complications to follow its use. Before the anæsthesia he injected scopolamine-morphine, for in his experience this is the only method of preventing the stage of excitation. Schmitz-Pfeiffer, as well as several others among the authors named above, pointed out that in Burkhardt's injections the ether solution must be introduced continuously, for otherwise the cannula may be blocked. The author regards the method of intravenous ether anæsthesia indicated in operations on the head and in cachectic persons.

In R. Vogelmann's opinion the intravenous method of ether anæsthesia is inconvenient and not likely to replace general anæsthesia, though it may be a useful auxiliary to the latter. The method has advantages, however, among which are calm sleep, the absence of fear and repugnance to the anæsthetic, while the stage of excitation is absent, and there is no primary irritant effect on the respiration and on the heart. The blood pressure is practically unaltered, and there are no after effects. The dosage may be accurately adjusted, and it is a convenient method from the anæsthetist's point of view, particularly in operations on the neck and face. Absolute contra-indications to its

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Pikin, Zentralblatt für Chirurgie 1910, No. 19.

Schlimpert, Zentralblatt für Gynäkologie 1910, No. 25.

Brüning, Münchener medizinische Wochenschrift 1910, No. 22, p. 1176.

Clairmont - Denk, Wiener klinische Wochenschrift 1910, No. 8, p. 286.

Schmitz - Pfeiffer, Medizinische Klinik 1910, No. 22, p. 882. —

Deutsche medizinische Wochenschrift 1910, No. 40, p. 1887.

Vogelmann, Dissertation, Heidelberg 1910. — Münchener medizinische Wochenschrift 1910, p. 2107.

use are advanced changes in the vascular system, and general plethora. Further, severe kidney disease and disease of the respiratory organs necessitates care, and caution is also required in operations in which the pelvis has to be considerably raised.

P. Sudeck considers ether anæsthesia to be the only perfectly safe method of anæsthesia which may be applied without assistance. In skilful hands the interference with respiration that appears at first may be completely prevented. To this end the author recommends that the anæsthetic be admitted drop by drop to begin with, and at an accelerated rate later on. The application of morphine and scopolamine may be advantageously combined with this method. The total quantity required amounts to 5 to 25 grammes. Particular attention should be given to recognising the moment at which the operation may be begun, and the author gives full directions on this point. In the ideal ether anæsthesia the patient should neither lose his knowledge of where he is nor his power of feeling. He hears every word, does as directed, gives correct answers, is completely awake and bright immediately the mask is removed, and is able to describe the operation that has been performed upon him. Sudeck considers ether anæsthesia to be indicated in all operations which cannot be performed under local anæsthesia either for local or for psychical reasons, and which can be speedily concluded. He recommends it particularly for extracting teeth, for painful dressings, and for reducing fractures. Of more prolonged operations those are particularly suitable in which it is desirable to retain the reflexes, e. g., excision of the jaw. Landström has given a trustworthy indication with regard to the recognition of the proper moment to begin the operation. He found that the increased secretion of saliva produced by the ether led to reflex movements of swallowing which at first were repeated at regular short intervals. The moment at which the intervals of swallowing become longer, indicating that the patient is no longer reacting to the salivation, is regarded by him as marking the advent of anæsthesia.

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Sudeck, *Archiv für klinische Chirurgie* 1909, No. 2. — *Zentralblatt für die gesamte Therapie* 1910, p. 258.  
Landström, *Zentralblatt für Chirurgie* 1909, No. 44.



Other communications on the value of ether hemi-anæsthesia are given by V. Schiller who confirms Sudeck's statements, and has made a special study of the method of prolonging the hemi-anæsthesia after it has been produced by Sudeck's method. He gives directions for this, as well as the indications. As these cannot be reproduced in abstract, the original paper should be consulted.

J. E. Engstad reports that ether gives good results as an antidote for cocaine and stovaine poisoning. The author used the remedy in the form of inhalations as in anæsthesia, and in the same doses. He attributes the action of ether to its stimulant effect on the nervous system and on the cardiac muscle. It is also undoubtedly due to the increased rate of circulation in the lungs.

Quénu found ether to be a valuable substitute for chloroform for anæsthetic purposes in diseases of the liver with jaundice. The day following the use of chloroform the jaundice and the symptoms of biliary intoxication are said to be increased, while this is not the case when ether is used.

### **Æthyl chloridum.**

The advantages of ethyl chloride in general anæsthesia are explained by Miller in a comprehensive paper. He points out the convenience and economy of ethyl chloride anæsthesia, and emphasises particularly the rapid onset of anæsthesia and the speedy recovery after its use. The preparation has a more agreeable effect on the patients than other anæsthetics, its odour is more pleasant than that of ethyl ether and the choking sensation of the latter is not observed. In Miller's experience patients who have been anæsthetised both with ethyl chloride and ethyl ether always ask for ethyl chloride. When treated with the latter patients first experience a slight sensation of giddiness, whereupon they fall into a quiet sleep. Elderly persons, partic-

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Schiller, Wiener klinische Wochenschrift 1910, p. 812.

Engstad, Journal of the American Medical Association 1910, No. 12.

— Klinisch-therapeutische Wochenschrift 1910, p. 417.

Quénu, Deutsche medizinische Wochenschrift 1910, No. 38, p. 1784.

Miller, Boston Medical and Surgical Journal 1909. — Zentralblatt für die gesamte Therapie 1910, No. 5, p. 259.

ularly those with calcareous degeneration of the arteries, stand ethyl chloride excellently; so do children, who find the odour of the remedy very agreeable. A further advantage over ethyl ether is the fact that ethyl chloride does not irritate the air passages and the kidneys, it does not produce cyanosis and does not cause copious secretion from the mucous membranes as is the case with ethyl ether. In operations lasting longer than three minutes the author uses ethyl chloride until unconsciousness has set in, when he continues the anæsthesia with ethyl ether. He has successfully obtained anæsthesia lasting for as long as 20 minutes by means of ethyl chloride alone. In Miller's opinion this method of anæsthesia requires great care and considerable practice, for any possible danger is not easy to recognise. In the hands of a skilled anæsthetist ethyl chloride anæsthesia is more reliable than ether anæsthesia, but is not so certain as nitrous oxide gas, though it is cheaper than the latter. Miller reports several cases, however, in which ethyl chloride had been used in larger quantity than was necessary. In several of these cases respiratory disturbances were set up within the first 5 minutes of the anæsthesia. On discontinuing the anæsthesia and performing artificial respiration normal respiration began again and the operation was completed without further interruption. A very favourable feature of this complication of ethyl chloride anæsthesia was the fact that the pulse continued good and that the patient rapidly recovered.

Lotheissen obtained good results with the combined inhalation of ethyl chloride and oxygen. In no case did he observe injury to the lungs or the kidneys. He considers the preparation particularly suitable for anæsthetising delirious patients, drunkards and those with psychic maladies.

### **Æthyleni chloridum.**

Ethylene chloride, also known as ethylene dichloride,  $\beta$ -dichlorethane, elayl chloride, is a colourless fluid with an odour resembling that of chloroform; specific gravity 1.265, boiling point  $84^{\circ}$  C. Its chemical formula is  $\text{CH}_2\text{Cl}-\text{CH}_2\text{Cl}$ . This drug has already found extensive use as a substitute

for chloroform. Recently A. J. Wallace recommended it for disinfecting the skin. The author points out that the use of a solution of iodine in acetone\*) has the disadvantage that when applied to large areas of skin, vapours are generated which irritate the respiratory organs. On the other hand the bactericidal power of a solution of iodine in acetone is greater than that of a solution of iodine in alcohol. For these reasons the author feels justified in seeking other solvents for iodine for this purpose. He considers ethylene chloride the most suitable preparation, particularly as it is said to be considerably superior to acetone as an agent for dissolving fat. The 2.48 p.c. solution (a saturated solution at ordinary temperature) has a dark violet colour, and a slight smell, while it does not inflame the mucous membranes. When applied to the skin it dries rapidly, producing only a slight pricking sensation. The skin is treated with this solution before the operation, after rubbing with a mixture of equal parts of alcohol and ethylene chloride. Dermatitis was never observed by Wallace after the use of iodine-ethylene chloride solution. The iodine-ethylene chloride solution must be kept in well stoppered bottles, protected from light, for ethylene chloride, like chloroform, is decomposed by exposure to air and light.

### Afridol.

Afridol, according to Schrauth and W. Schoeller, is the name of a complex mercury compound, oxy-mercury-o-toluylic sodium. It is a disinfectant and increases the disinfectant power of soaps, particularly of those rich in palmitin, stearin and tripalmitin. It has the advantage over mercuric chloride of not decomposing in the presence of alkaline soaps, so that it appears particularly well suited for the preparation of mercurial soaps. A soap of this kind is issued under the name of afridol soap. The investigations of the above authors prove that this soap is a reliable substitute for corrosive sublimate soaps, which are unsuitable both from the chemical and practical point of view. Afridol is free from all the disadvantages that limit the practical use of mercuric chloride. Afridol (and

Wallace, British Medical Journal 1910, No. 2578, p. 1288.

\*) See Merck's Reports 1909, p. 85.

Schrauth-Schoeller, Medizinische Klinik 1910, No. 36.



afridol soap) is a complex compound of mercury which does not attack metals, so that it may be used not only for disinfecting the hands but also for disinfecting the instruments for use in operations. As compared with lysol and such preparations, it is said to have the further advantage of possessing a greater disinfectant power, while it is free from smell. Further, afridol and afridol soap have no irritant action on the skin, so that their use should be considered in parasitic and bacterial diseases of the skin and hair.

### Alcohol.

The alcohol compresses of Salzwedel do not as yet appear to have received the attention they deserve. Recently they have been recommended in the communications of C. Köhler and Cheinisse. Köhler points out the value of alcohol dressings in incipient inflammatory processes such as cellulitis, whitlow, mastitis, phlebitis, lymphadenitis, etc., in their initial stage; their application usually causes the pain to disappear with surprising rapidity, while the inflammation subsides. He considers alcohol to be useful even after suppuration has begun, if necessary the pus is first removed; this treatment accelerates healing after operations. He found the alcohol applications very useful in carbuncles, inflamed glands, especially inguinal glands, also in orchitis, epididymitis, erysipelas, bruised ribs, herpes zoster, neuralgia, tonsillitis, inflamed joints and chronic rheumatism. The mode of application of alcohol compresses is very simple. The inflamed part is covered with 10 layers of gauze soaked in alcohol 90 p. c., the dressing being large enough to extend a hand's breadth beyond the affected part. The gauze is covered with gutta percha tissue and this with a good layer of cotton wool, and the dressing is renewed every 4 hours. In the case of a sensitive skin alcohol 70 p. c. is used, and the skin may be rendered less sensitive by sprinkling talc upon it. In articular rheumatism and in neuralgia, Köhler uses warm alcohol at the beginning of the treatment. Cheinisse obtained very satisfactory results by the application of alcohol dressings in typhoid fever. In this case it is imperative to cover the whole abdomen with

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Köhler, *Therapie der Gegenwart* 1910, No. 8, p. 379.

Cheinisse, *Semaine médicale* 1910, No. 46, p. 541.

gauze saturated with alcohol. To lessen the irritant action of alcohol the author applied, over the alcohol compress, a layer of cotton wool soaked in cold water, over which he applied the other materials mentioned above. The layer of cotton wool is renewed every hour, the alcohol compress every two hours. In less severe inflammation of the skin, Cheinisse has successfully applied lanolin, which permits a continuance of the application of alcohol dressings.

W. Harris and Landete have reported on the treatment of trigeminal neuralgia with alcohol injections. The results obtained by Harris were so good that he considered the effects almost as good as those obtained by resecting the Gasserian ganglion. The neuralgia disappeared permanently, or if it returned it could be kept away for months by renewing the alcohol injections. The dose is 1 to 1.5 c.c. of alcohol (90 p.c.) Landete injected 1 c.c. of alcohol in a case of facial neuralgia, and cured the malady completely; at any rate there was no relapse after a year.

Alcohol is of special interest in the disinfection of the hands. Kutscher attributes its action to four properties: of dissolving fat and loosening epidermis, acting as a mechanical cleanser, while causing shrinking and fixing. In his opinion no bactericidal action is displayed. H. Selter, however, attributes a high bactericidal power to alcohol. This can be increased by combining it with soap and thereby enabling the alcohol to reach the deeper pores of the skin where it destroys the germs. This combination is prepared by dissolving 14 parts of hard soap in 86 parts of absolute alcohol by the aid of heat. An alcohol paste is obtained in this way, which is solid at ordinary temperature. 20 grammes ( $\frac{2}{3}$  oz) of it rubbed into the skin of the hands for 5 minutes are as effective a disinfectant as 150 c.c. (5 oz) of absolute alcohol. Schumburg is not in favour of previously washing the hands with soap. The absolute alcohol is, in his experience, the most essential feature

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Harris, British Medical Journal 1910, No. 2580, p. 1404.

Landete, Revista de Medicina y Cirurgia 1910, April 14.

Kutscher, Veröffentlichungen aus dem Gebiete des Militär-Sanitätswesen 1910, No. 44.

Selter, Deutsche medizinische Wochenschrift 1910, No. 31, p. 1563.

Schumburg, Deutsche medizinische Wochenschrift 1910, No. 23, p. 1075. — See Merck's Reports 1908, p. 117.

of this method of disinfection. There is no advantage in adding ether, acetone, nitric acid or formaldehyde, for the results obtained by doing so are no better.

### **Alcohol amylicum.**

Amyl alcohol has been shown by recent investigations of Horand to have a disinfectant and desiccating action, rendering it suitable for the treatment of ulcerating inoperable carcinomata. If undiluted amyl alcohol be dropped upon a carcinomatous growth a copious excretion of fluid is produced which brings away a considerable number of dead parasites. The further use of the remedy causes the tumour to shrink, its borders become less raised, and the nauseous smell is completely abolished. Horand states further that the use of amyl alcohol causes a discharge of toxins, and thus leads to a considerable improvement in the general condition, particularly with regard to appetite and sleep. In a case of ulcerating mammary carcinoma treated without success by Röntgen rays, the author states that he obtained a diminution in the growth, and in the case of an inoperable cancer of the penis he obtained so considerable an improvement that an operation could be successfully undertaken. The treatment depends in the main in pouring increasing doses (3 to 10 drops) upon the tumours twice a day.

A reaction for amyl alcohol, the chief object of which is to detect fusel oil in cheap brandy and thus to prevent poisoning from the consumption of such brandy, has been given by H. Holländer. It is well known that small quantities of amyl alcohol, when introduced into the organism frequently or regularly with brandy, cause a particularly harmful form of alcoholic intoxication. The method of analysis suggested by Holländer is as follows. To 25 c. c. of the brandy to be tested 1 c. c. of normal potassium hydroxide solution is added. The mixture is distilled, and 5 c. c. of concentrated acetic acid are added to 5 c. c. of the distillate. This mixture is heated to boiling for one minute when a drop of pure phenyl-hydrazine is added. The clear solu-

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Horand, *Journal des praticiens* 1910, No. 19. — *Revue de thérapeutique* 1910, p. 448.

Holländer, *Münchener medizinische Wochenschrift* 1910, No. 2.



tion is then boiled once more and placed in iced water until it has cooled to the ordinary temperature. The cooled mixture is carefully "layered" on to concentrated sulphuric acid, when the presence of amyl alcohol in the fluid to be tested is apparent by the appearance, at the point of contact of the two fluids, of a ring of a more or less intense green colour. Occasionally a brown colour also appears above this ring, but this has no bearing on the result of the test.

### Allosan.

Recent investigations have established that allosan, the allophanic ester of santalol\*), is a useful remedy for gonorrhœa. MacCracken advocates the simultaneous internal and local treatment of gonorrhœa, and he regards the combination of protargol treatment with the administration of allosan as a successful method of treating gonorrhœa. The preparation has a decided sedative action which shows itself in the rapid subsidence of the pain on micturition and the cessation of nocturnal erections. It also has anti-catarrhal properties which are apparent in the early cessation of the discharge. Finally it has the power of preventing a general infection as well as arthritic complications.

A. Regenspürger has studied the therapeutic properties of allosan more fully. He used allosan tablets, each of which consists of 0.5 gramme ( $7\frac{1}{2}$  grains) of allosan and 0.2 gramme (3 grains) of starch. He gave 1 or 2 of these for a dose, or 4 to 8 a day, though if necessary 12 tablets may be given daily without harm. He only prescribed allosan when there was a definite indication for the use of balsams. Thus in all cases of acute and subacute gonorrhœa of the anterior urethra, in catarrhal urethritis, in acute exacerbations of chronic gonorrhœa, in extension of the acute process to the posterior urethra and the bladder, and in other acute complications such as prostatitis, epididymitis and lymphangitis dorsalis. In the two latter conditions very energetic internal treatment is indicated, particularly if local treatment has to be discontinued. In other cases Regenspürger is in favour of the simultaneous internal and local

\*) See Merck's Reports 1908, p. 118.

MacCracken, Medical Press and Circular 1909, May 5. —

Deutsche Medizinal-Zeitung 1910, No. 16, p. 286.

Regenspürger, Medizinische Klinik 1910, No. 8, p. 307.

treatment of gonorrhœa. For local use he prefers novargan to other organic silver preparations because it is non-irritant and possesses a high bactericidal power. The only contra-indications for allosan mentioned by him are severe gastro-intestinal diseases, and nephritis in all stages. The cases described by this author point to allosan being a useful substitute for the well known balsams, while it has the advantage, as compared with the latter, that it can be given in the form of powders or tablets. It communicates no smell to the breath, and it may be used even in cases of idiosyncrasy to balsams.

Erdös mentions as a special advantage of allosan its freedom from taste and its freedom from irritant action on the stomach and intestines, and on the kidneys and bladder. In acute cases he observed that the administration of allosan was followed by a diminution of the discharge even before local treatment had been commenced, while in posterior gonorrhœa the further progress of the complaint was checked, though no cure was obtained. The preparation also gave good results in cystitis in bedridden patients, diminishing the pain on micturition and the amount of pus in the urine, while it rendered the urine acid within a few days. In epididymitis and orchitis the author's results were less satisfactory.

O. Scheuer and Jourdan agree on the whole with the conclusions of the above authors, and consider allosan to be a valuable adjuvant in the treatment of gonorrhœa.

### **Aluminii aceto-tartras.**

The use of this remedy in dermatological practice is described in a communication by M. Lewitt which is of interest for the reason that little has been written as yet on the use of this preparation in cutaneous and sexual troubles\*). Lewitt particularly recommends the use of the so-called alsol ointment, a cream containing 0.5 p. c. of aluminium aceto-tartrate in aqueous solution. The author found

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Erdös, Pester medizinisch-chirurgische Presse 1910, No. 15.

Scheuer, Österreichische Ärzte-Zeitung 1910, No. 12, p. 263.

Jourdan, Bulletin général de thérapeutique 1910, August. —

Revue de thérapeutique 1910, p. 643.

Lewitt, Therapie der Gegenwart 1910, No. 2, p. 95.

\*) See Merck's Reports 1900 and 1903.

it to be not merely a mild and cooling application, but absolutely non-irritant, while it does not turn rancid and does not lose its action on keeping. It is indicated in cutaneous affections coupled with troublesome itching, in intertrigo, moist dermatitis and acute eczema, in which it relieves the subjective troubles, such as the burning and the pain. In acne vulgaris Lewitt opened the pustules and applied alsol cream with the result that no further spots appeared, nor was irritation set up, as often follows the use of ointments. In various forms of dermatitis he obtained good results with the use of this cream. In cases of idiosyncrasy to fats and ointments he recommends the use of alsol in the form of a dusting powder. He used alsol cream with good results in erythema exsudativum multiforme, in furuncles to protect their vicinity from infection, in hyperidrosis after bathing and washing with aluminium acetate, in impetigo contagiosa after removal of the crusts, in intertrigo, burns and ulcers of the leg. In gonorrhœa in the female, Lewitt used a solution consisting of a mixture of one tablespoonful of liquor alsoli (a 5 p.c. aqueous solution of aluminium aceto-tartrate) in 1 litre of lukewarm water. Tampons were then applied which had been soaked in a 1 p. c. solution and allowed to dry, or alsol ointment on a tampon was applied. In simple cases of fluor albus good results were also obtained by irrigation with a 0.5 p. c. solution. Finally the author points out that alsol gives good results in the local treatment of syphilitic diseases of the mucous membranes of the mouth and throat, in mercurial and aphthous stomatitis, in scorbutic affections of the gums, and as a prophylactic mouth wash during courses of mercury treatment.

### Alypin.

The use of alypin as a local anæsthetic has been described by Hamm, A. Bubenhofer, P. Fleissig, Eisert and W. Peters.

In minor surgery, e. g., in the extirpation of small tumours, the removal of foreign bodies, tracheotomies, and

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Hamm, Deutsche medizinische Wochenschrift 1910, No. 25.

Bubenhofer, Münchener medizinische Wochenschrift 1909, No. 42.

Fleissig, Medizinische Klinik 1910, No. 5.

Eisert, Zahnärztliche Rundschau 1910, No. 30.

Peters, Deutsche zahnärztliche Wochenschrift 1910, No. 10.



particularly in operations on the fingers and toes, Bubenhofer used a 1 p.c. solution of alypin to which were added 3 to 5 drops of a 0.1 p.c. suprarenin solution. Of this he injected 1 to 2 c.c. (17—34 min.) whereupon the required degree of anæsthesia of the affected part was obtained within a minute. The injection was made 2 cm. ( $\frac{4}{5}$  in.) from the point selected for the operation. In operations on the first phalanx he made the injection at its base immediately in front of the metacarpo-phalangeal joint. For amputating fingers he found that 4 c.c. (68 min.) of the solution were required.

Hamm used a 5 p.c. solution, of which he injected 0.5—1 c.c. ( $8\frac{1}{2}$ —17 min.) at the seat of the proposed operation, for opening abscesses, furuncles and small phlegmons, and obtained complete anæsthesia.

Fleissig, in a review of the results reported in the literature on alypin, also mentions the experiences of Iselin. According to his account satisfactory anæsthesia was always obtained in a large number of small operations such as cuts, suturing tendons, amputating fingers, extirpating lipomata, sebaceous cysts, dermoids, nævi, carcinoma of the skin, ganglia, lymphomata, etc., and in removing foreign bodies. As a rule 2 to 8 c.c. of a 0.5 p.c. solution of alypin were applied, to which 2 drops of a 0.1 p.c. suprarenin solution were added before injection. No symptoms of intoxication or painful after effects were observed, and in two cases only of exploratory incisions was there necrosis of the skin at the seat of the injection.

In dental operations alypin also gives good results, as appears from the reports of Bubenhofer, Eisert and Peters. Bubenhofer used ampoules containing 1.3 c.c. of a 2 p.c. solution. In the extraction of molars or premolars he injected the contents of one ampoule, in cases of spongy gums  $1\frac{1}{2}$  ampoules. Peters used alypin tablets containing 0.05 gramme ( $\frac{3}{4}$  grain) of alypin and 0.00033 gramme ( $\frac{1}{200}$  grain) of suprarenin. In mandibular anæsthesia he dissolved 1 tablet in 2 c.c. of water. For regional anæsthesia one tablet was dissolved in 6 c.c. of water, and of this solution 2 c.c. were injected into the mouth at the reflection of the mucous membrane, 0.5 c.c. in the palate, so that altogether about 0.025 gramme ( $\frac{2}{5}$  grain) of alypin was injected. This dose is sufficient for several adjacent teeth, provided the fluid is injected slowly over the various teeth. In mandibular

anæsthesia it is necessary to wait 25 to 30 minutes, in regional anæsthesia 3 to 5 minutes.

H. Fischer reports on several methods of producing anæsthesia with alypin that have given good results in practice. He also confirms the usefulness of alypin in various branches of surgery.

### **Amido-azotoluol medicinale.**

Amido -azotoluol, as is well known, has been said by Hayward to possess the same power as scarlet red\*) in furthering epithelial growth. F. Grossmann has investigated its action more fully and reports his results from its use in otology. Grossmann is of opinion that the application of the remedy in the form of an ointment is of no use, and he recommends instead the use of gauze soaked in a 4 p. c. alcoholic solution of amido-azotoluol (epithermol gauze). In the after treatment of cavities subsequent on total extirpation by chiselling and after operations on cavities in the jaw, it is said to be of good service in furthering the growth of epithelium. In the treatment of chronic suppuration in which the epidermis grows so as to invade the handle of the malleus in the tympanic cavity where it is fixed to the promontory, Grossmann recommends the use of amido-azotoluol solution in absolute alcohol or in lactic acid. In old perforations it is advisable, before applying the remedy, to refresh the edges of the perforation. Instead of gauze or ointment a powder may be used consisting of amido-azotoluol and boric acid.

For the treatment of wounds, W. Katz prefers amido-azotoluol to scarlet red as its action is more reliable while it does not stain the clothing to such an extent as the latter. The author obtained very satisfactory results in a large number of cases including whitlow, wounds following cellulitis and incisions for abscesses, buboes, mastitis, laparotomy and amputation wounds when they do not heal by first intention, varicose and syphilitic ulcers of the leg, burns, etc. In every case

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Fischer, Deutsche medizinische Wochenschrift 1910, No. 38.

Hayward, Münchener medizinische Wochenschrift 1909, p. 1836.

— See Merck's Reports 1909, p. 105.

\*) See Merck's Reports 1908, p. 289 and 1909, p. 306.

Großmann, Zeitschrift für Ohrenheilkunde 1910, p. 415.

Katz, Deutsche medizinische Wochenschrift 1910, No. 36, p. 1665.

he used an 8 p. c. amido-azotoluol ointment. He found that a favourable effect was only obtained if the ointment was applied to granulations that had been previously thoroughly cleansed. In ulcerating wounds it may even increase the discharge and impede the growth of epithelium. In small wounds of the size of a shilling a single application is occasionally sufficient, but in larger wounds it is necessary to change the dressing fairly often, and to alternate the treatment with the application of a neutral ointment to prevent exuberant granulations. The amido-azotoluol ointment is spread on gauze, and its application is limited to the granulations. In this way inflammation of the healthy skin is avoided.

### **Ammonii molybdas.**

A new reagent for glue, which would undoubtedly be equally applicable to the determination of gelatin, is described by E. Schmidt. If an aqueous solution of ammonium molybdate is added to a solution of glue, and acidified by the addition of a mineral acid, a dense white precipitate is produced, which after some time assumes a slightly bluish-green colour, as a result of the reduction of the molybdic acid. The fluid above the precipitate also acquires this colour after a time. The precipitate is soluble in concentrated hydrochloric acid and in nitric acid, less soluble in sulphuric acid, and only slightly soluble in acetic acid (80 p. c.). Other substances such as gum acacia, egg albumin, dextrin and mucilage of linseed do not give this reaction, or they produce merely a slight turbidity. As a reagent for glue the author recommends a solution of 3 grammes of ammonium molybdate in 250 c. c. of water and 25 c. c. of nitric acid (Sp. G. 1.2). Further experiments will show whether this reaction is suitable for the quantitative estimation of glue.

### **Anthrasol.**

A publication by Ch. A. Edelen on anthrasol in dermatological practice shows that the author recognises

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Eugen Schmidt, *Chemiker-Zeitung* 1910, p. 839.

Edelen, *Medical Progress* 1909, October. — *Allgemeine medizinische Zentral-Zeitung* 1910, p. 158.



the advantages of this remedy as a substitute for tar, of which mention has already been made in these Reports. In consequence of being colourless and viscous, it can be applied to all parts of the body. According to Edelen, the phenols contained in anthrasol allay itching and relieve pain, while the hydrocarbons exert a stimulating action. Like tar this preparation is particularly indicated in chronic diseases of the skin where its constituents are able to exert their effects to the full. Its oily character enables it to penetrate into the deeper layers of the skin and thus to accelerate the healing of the infiltrated parts. The author found it to be of particular value in eczema of the hands in workmen, when used in combination with oil and zinc oxide, in the place of chrysarobin in psoriasis in the form of a 20 p. c. ointment, in conjunction with the use of soft soap, and also in pruritus vulvæ et ani, pruritus universalis, scabies, etc., in which it relieves itching within a very short time. It is said to have been of good service also in a severe case of eczema papulosum of the legs.

### **Antiformin.**

The use of antiformin\*) as a disinfectant has been investigated experimentally by Fromme in the disinfection of stools. A somewhat surprising result was brought to light, viz., that the preparation is of little use for this purpose, and is inferior to several other disinfectants. The author found that a solution of crude caustic soda is a very useful substance for this purpose, and he considers that it deserves further investigation. Of course it is necessary, even in this case, to break up the fæces thoroughly so as to obtain a very complete mixture with the disinfectant. This is necessary in the case of all disinfectants, and the reason is obvious. We may safely assume, knowing the properties of solution of caustic soda, that no preparation is likely to allow of a more rapid and uniform mixture with the fæces than solution of caustic soda, particularly if it is used in a concentrated form. For this reason we can only support the recommendation to make further trial of solution of caustic soda.

\*) See Merck's Reports 1908 and 1909.

Fromme, Münchener medizinische Wochenschrift 1910, No. 15, p. 830.

E. Klebs has already published some communications with regard to the therapeutic use of antiformin\*). He found it both harmless and efficacious in many cases, particularly for disinfecting the skin, where it not only reduces the vitality of pathogenic germs but completely destroys them. For this purpose Klebs uses a 10 p.c. solution of antiformin; the hands are washed with it twice a day and before every operation. By this means Klebs found that the cutaneous microbes are completely destroyed before operations, especially diplococcus semilunaris or catarrhalis of Pfeiffer, and others. For disinfecting the mucous membrane a 1 p.c. antiformin solution is suitable, which is said to evolve a considerable amount of chlorine. As many patients find this unpleasant, Klebs has replaced the sodium hypochlorite of antiformin by sodium chlorate. Uhlenhuth has shown that this mixture also possesses the property of killing bacteria, though its action is weaker and slower.

The use of antiformin for the detection of tubercle bacilli has been mentioned by L. Lagrèze, Sachs-Mücke, W. Telemann, Schulte, Miessner and Kühne, K. Reicher, Krüger, H. Merkel, Görres, E. Bierotte, A. Skutetzky, H. Beitzke, C. Barile and Koslow. The antiformin method has already been

Klebs, Korrespondenzblatt für Schweizer Ärzte 1910, No. 5.

\*) See Merck's Reports 1909, p. 110.

Lagrèze, Deutsche medizinische Wochenschrift 1910, No. 2, p. 76.  
Sachs-Mücke, Deutsche medizinische Wochenschrift 1910, No. 7, p. 320.

Telemann, Deutsche medizinische Wochenschrift 1910, No. 19, p. 891.

Schulte, Medizinische Klinik 1910, No. 5, p. 172.

Mießner-Kühne, Mitteilungen des Kaiser Wilhelm-Institutes für Landwirtschaft 1910, p. 309. — Berliner tierärztliche Wochenschrift 1910, p. 730.

Reicher, Medizinische Klinik 1910, No. 21, p. 826.

Krüger, Münchener medizinische Wochenschrift 1910, No. 5, p. 270.

Merkel, Münchener medizinische Wochenschrift 1910, No. 13, p. 680.

Görres, Zeitschrift für klinische Medizin 1910, No. 2.

Bierotte, Berliner klinische Wochenschrift 1910, No. 19, p. 877.

Skutetzky, Wiener medizinische Wochenschrift 1910, No. 35.

Beitzke, Berliner klinische Wochenschrift 1910, No. 31, p. 1451.

Barile, Il moderno Zooiatro (Bologna) 1910, No. 10, p. 359.

Koslow, Russkij Wratsch 1910, No. 13. — Deutsche tierärztliche Wochenschrift 1910, No. 36, p. 541. — Berliner klinische Wochenschrift 1910, No. 25, p. 1181.

described in these Reports\*), and the works of these authors contain experiences which cannot be reproduced in abstract. Those who are interested in this subject should refer to the original papers.

### Antipyrine.

An antiseptic application for covering wounds and skin, the chief constituents of which are antipyrine and resorcin, has been suggested by Monteil. It is prepared by fusing together 188 grammes of antipyrine, 110 grammes of resorcin and 180 grammes of terpin hydrate at 125° C., preferably on an oil bath. This forms a glass-like mass on cooling, which is then dissolved in double its weight of glycerin. An ointment-like mass is thus obtained which resembles glycerin of starch in appearance. The preparation possesses antiseptic properties, and more than that, it relieves pain and checks hæmorrhage, while it is said to be completely non-irritant. A further advantage is found in the fact that it does not cause grease-spots, and that it can be washed away with water.

Bougault's work led Borde to work out a method of determining the iodine value of essential and fatty oils, superior in several respects to former methods. It is well known that J. Bougault showed that free iodine in an alcoholic solution is absorbed with loss of colour in the presence of chloride of mercury. He carefully examined the molecular changes occurring in this chemical action. It was found that iodine could be accurately titrated by means of antipyrine and conversely that antipyrine could be titrated by means of iodine. With appropriate alterations Borde used this method to determine the iodine value of essential oils. The determination can be carried out in alcoholic solution, so that the formation of layers as occurs with the use of sodium thiosulphate is avoided. The volumetric solution used by Borde is a 5 p. c. solution of iodine (in 95 p. c. alcohol), the strength of which is verified by the aid of an antipyrine solution (18.8 grammes of antipyrine in

\*) See Merck's Reports 1908 und 1909.

Monteil, *Süddeutsche Apotheker-Zeitung* 1910, p. 478.

Borde, *Süddeutsche Apotheker-Zeitung* 1910, p. 198.

Bougault, *Journal de pharmacie et de chimie* (6) Vol. 7, p. 161; Vol. 11, p. 97, 100 and 165.



a litre of 50 p. c. alcohol). In addition a solution is required of 6 grammes of chloride of mercury in 100 c. c. of alcohol (80 p. c.) To make the determination about 0.15–0.20 gramme (accurately weighed) of the fat or essential oil to be tested is placed in a glass-stoppered bottle of about 100 c.c. capacity, 10 c. c. of alcohol (95 p.c.) are added, also 10 c. c. of the above iodine solution and 10 c.c. of the chloride of mercury solution. The mixture is left in the dark. After 4 hours the iodine not absorbed is titrated with the antipyrine solution. The end of the reaction is readily recognised by the appearance of a slight yellow colour. 1 c.c. of antipyrine solution corresponds to 0.0254 gramme of iodine. In estimating fatty oils it is advisable to prepare all the solutions required with 95 p.c. alcohol so as to provide a clear fluid for titration. The iodine solution is best prepared fresh, for its titration value diminishes on prolonged standing; the antipyrine solution, however, will keep if stored in a well stoppered bottle.

### **Antituman.**

Starting from the fact that certain portions of the human body, such as the walls of the arteries and the cartilaginous ribs, are as a rule immune from cancer, R. Oestreich made experiments with a substance the chemical composition of which rendered it likely to exert an inhibitory influence on the growth of cancer cells, either by direct action on the cancer cells or by neutralising some substance excreted from these cells. For this purpose he selected chondroitin sodium sulphate which is issued in sufficient purity for therapeutic purposes under the name of "Antituman".

The author's antituman treatment consists in giving the patient subcutaneous injections once or twice a day of 0.1 gramme of antituman in sterile aqueous solution, in some part of the body, not necessarily in the region of the tumour. In the second week of the treatment the dose may be raised to 0.2 gramme. After 4 to 6 weeks' treatment the injections are discontinued for 1 to 2 weeks, when the treatment is recommenced. This treatment has only been used by the author in hopeless cases of mammary, gastric, rectal and

uterine carcinoma, and hitherto he has confined its use to inoperable, completely hopeless patients in whom he has observed the following effects: In several patients every injection was followed, after 1 to 2 hours, by severe pain lasting an hour on an average, and limited to the cancerous part. He regards this as a sure sign that there is really an action due to the remedy on the cancerous part. This view is all the more probable since the pains do not occur when the injections are discontinued. No harmful effect following antituman injections was observed in any case.

His clinical observations have led Oestreich to assume that antituman has a definite action on the organ affected by cancer, and on the body of the patient. The action on the affected organ shows itself by the cessation of the growth of the carcinoma, and on the patient by the improvement in the general condition. The action of the remedy was also apparent in the post-mortem examination of fatal cases. Thus in cases where antituman injections had been given for more than 4 weeks the author found that small metastatic cancerous nodules which were not ulcerating were filled with a considerable quantity of polynuclear leucocytes, while degeneration and necrosis had occurred in the masses of cancer cells. These changes may be regarded as evidence of a reaction. The author therefore recommends his method for further trial, and suggests treatment with antituman in every case after the operation wound has healed, for the good effect of the remedy, if there be really a good effect, in the majority of cases would be apparent in the absence of relapses and metastases. He further recommends the treatment of inoperable cases with antituman, for in his experience they are certainly benefited, although it is not to be expected that a stomach or a liver destroyed by cancer can be completely healed.

### **Aperitol.**

Clinical reports on the use of aperitol have been published by A. Hirschberg and K. Pronai. Hirschberg used the preparation for several months in a large number of patients, and on the whole confirms the good properties

Hirschberg, *Therapie der Gegenwart* 1910, No. 7, p. 334.

Pronai, *Wiener klinische Rundschau* 1910, No. 1, p. III.

of this new purgative, as described by other authors\*). It is a matter of experience that a tendency to constipation is greater in women than in men, and the dosage must be adjusted accordingly. For men Hirschberg found that 1 to 2 tablets were usually sufficient to obtain the desired result, while for women 2 to 3 tablets are required. Aperitol is readily taken by women, and in the author's experience it never caused pain on evacuation. A motion was obtained about 6 to 7 hours after taking the remedy, and neither irritant nor toxic symptoms were observed. Even larger doses (4 to 5 tablets) were borne without trouble. Aperitol is best taken at bedtime or in the morning. Pronai prescribed aperitol in 326 cases (to women) and confirms its usefulness in many cases in which dietetic and physical measures are not applicable. With 2 to 3 tablets he found that a painless motion could be produced in the majority of cases. The remedy rarely fails, and three-quarters of the patients thus treated stand it without pain. In the other cases the sedative component of aperitol, the valerian, (though not too weak) is apparently not suitable. Pronai cannot give any method of ascertaining to which cases this applies. The first evacuation occurs as a rule after 8 hours, in pregnant women perhaps rather later, though not infrequently it is necessary to wait more than 15 hours for the effect. In two-thirds of the cases 1 to 2 motions are obtained, occasionally more. In two-thirds of the cases a pultaceous first evacuation is to be expected, in other cases the motion is fluid, rarely hard. We are not to expect a permanent regulation of the motions any more than we are to expect a permanent disturbance of the intestinal function. Occasionally constipation is transitorily produced, although this sequel does not follow diarrhœa with any particular frequency. Even after 8 tablets have been taken no damage to the organism is observed. Pronai has ascertained further that after the use of aperitol no phenolphthalein is present in the mother's milk, so that diarrhœa occurring in the infants cannot be attributed to aperitol taken by the mother.

Szereszewski is very satisfied with the action of aperitol. In constipation with bleeding anal fissure, in constipation during pregnancy, after radical operation for stran-

\*) See Merck's Reports 1908 and 1909.

Szereszewski, Fortschritte der Medizin 1910, No. 43.



gulated inguinal hernia, in acute and chronic nephritis, painful hæmorrhoids, etc., the remedy produced a painless motion. A great advantage of aperitol is said by the author to be the fact that in chronic constipation it is not necessary to increase the dose of the remedy, since no habituation to it is produced. It is particularly useful in the presence of anal fissures, hæmorrhoids, chronic colitis and dysentery in which the motions are as a rule accompanied by pain and tenesmus.

Ch. E. Buck also confirms the value of aperitol in constipation.

### **Apomorphinæ hydrochloridum.**

In Harnack's publications attention was drawn to the fact that an impure commercial apomorphine hydrochloride is sometimes met with which is unsuitable for therapeutic use. For this reason it is of interest to review the tests applicable to apomorphine hydrochloride.

To detect the presence of foreign alkaloids Frerichs gives the following method: 0.1 gramme of apomorphine hydrochloride is placed on a small, dry filter and 5 c. c. of a mixture of one part of hydrochloric acid and 4 parts of water are poured on to the salt. Solution of potassiummercuric iodide is added to the filtrate. Pure apomorphine hydrochloride gives rise to no more than an opalescent turbidity. If other alkaloids are present in the preparation which are soluble in hydrochloric acid (morphine, etc.) the above reagent causes a precipitate.

Boehringer recommends the following test for  $\beta$ -chloro-morphide: 0.1 gramme of apomorphine hydrochloride is dissolved in 10 c. c. of water, 20 c. c. of ether are layered over the solution and 5 c. c. of a cold, saturated solution of sodium bicarbonate are added, and the mixture is shaken until the precipitate which is formed is dissolved. The aqueous solution is withdrawn, the ether is then washed 3 times with 20 c. c. of water each time, and is then evaporated

Buck, Deutsche Medizinalzeitung 1910, No. 48.

Harnack, Münchener medizinische Wochenschrift 1910, No. 1, p. 20 and No. 33, p. 1745. — Pharmazeutische Zeitung 1909, No. 95, p. 938 and 1910, No. 69, p. 693.

Frerichs, Apotheker-Zeitung 1909, No. 99, p. 928.

Boehringer, Chemiker-Zeitung 1910, No. 100, Repertorium p. 410, Pharmazeutische Zeitung 1910, No. 57.

to dryness in a test tube. 5 c.c. of concentrated nitric acid containing 0.5 p.c. of silver nitrate are added to the residue on cooling. After 10 minutes the test tube is placed in a water bath at boiling point for 1 hour. At the end of this time the clear undiluted brown fluid should contain no perceptible particles of chloride of silver, or at most they should be extremely minute.

### **Arecolinæ hydrobromidum.**

From a comprehensive pharmacological paper by W. Pätz we extract certain data of general interest. One of the most important points is the author's result regarding the stability of arecoline hydrobromide. He found that after standing for several years the preparation showed no change in its chemical and physiological properties. In a non-sterilised solution, however, it began to lose its pharmacodynamic power at the end of four weeks. Pätz showed further that solutions of arecoline lost none of their efficacy when sterilised.

Regarding the antagonism between arecoline and atropine the author reports that atropine, even in doses insufficient to paralyze the normal intestine, prevents all excitation of the intestinal movements produced by arecoline, the stimulant action due to the arecoline when administered is here of no importance. Further, the action of arecoline when administered after atropine is weakened to such a degree that very large doses of arecoline are necessary to produce even a limited stimulant effect. If the bowel has been completely paralyzed by atropine, even large doses of arecoline give rise to no movements. Morphine does not produce the same effect as atropine, for it does not diminish either the amount or the course of the excitation produced by arecoline. However, the bowel excited by arecoline may be completely set at rest by extract of opium\*).

### **Argenti acetas.**

The use of silver acetate in the treatment of gonorrhœal ophthalmia has been described by Scipiades. It is

Pätz, Zeitschrift für experimentelle Pathologie und Therapie 1910, No. 3, p. 577.

\*) The author's experiments were all performed on the isolated intestines of cats.

Scipiades, Pester medizinisch-chirurgische Presse 1910, No. 27.

well known that Zweifel some time ago recommended silver acetate in place of silver nitrate because it is less irritant, and at ordinary temperature it is only soluble up to a certain concentration. Hence it is not possible for a solution kept in an improperly stoppered bottle to become so concentrated by evaporation as to be unsuitable for the treatment of the eyes. With silver nitrate this may readily occur. In the Women's Clinic of the University of Munich a 1-2 p. c. solution of silver acetate has been used with success for the past six years\*). This means a saturated solution at 30°C., and was selected for the reason that it was desired to use a solution which is saturated at all temperatures concerned. At lower temperatures a little silver acetate separates out, but this does no harm. On the other hand a solution of silver acetate, even if kept at 0°C., still contains sufficient silver acetate (about 0.7 p.c.).

The results obtained by Scipiades at the Women's Clinic in Pesth show that silver acetate solution is superior to a solution of silver nitrate\*\*).

### Argenti nitras.

M. Baruch combined silver nitrate and kaolin and obtained an excellent preparation for the treatment of wounds; it not only promoted granulation in the way many antiseptic preparations do, but also stimulated epithelial growth considerably. The action of kaolin and its value in the treatment of wounds may be said to be well known\*\*\*). Recent wounds are very rapidly brought to heal. In larger wounds, when crusts or spongy granulations appear, Baruch recommends the addition of powdered silver nitrate. Baruch gives the following prescription:

Rp. Argent. nitr. 1.0 gramme (15 grains)

Kaolin. steril. ad 100.0 grammes (3 $\frac{1}{3}$  oz)

M. Fiat pulv. subtil. D. in vitr. nigr.

This powder was used by the author in various kinds of wounds, after the extirpation of a cancrroid, in the wound

Zweifel, Zentralblatt für Gynäkologie 1900, No. 51.

\*) See Therapeutische Monatsberichte 1910, No. 7.

\*\*) See Merck's Reports 1901, 1903, 1906 and 1907.

Baruch, Münchener medizinische Wochenschrift 1910, No. 35, p. 1829. — Semaine médicale 1910, No. 40, p. 478.

\*\*\*) See the article "Bolus Alba" in these Reports.



left after a carcinoma operation, in traumatic gangrene, furuncles, whitlows, in incised wounds, teno-synovitis and in burns. The results of the treatment showed that silver nitrate-kaolin is a mixture which very rapidly cleanses unhealthy looking wounds covered with pus and fibrin, and frequently 1 or 2 days suffice to give the wound a clean appearance. Even necrotic areas loosened within a few days and were thrown off, followed by a considerable production of healthy red granulations and a rapid growth of epithelium. This was particularly evident in the case of burns.

To apply the powder it is best to use a sprinkler which may be made by covering the mouth of a wide-necked brown bottle with wide meshed gauze. Enough powder is spread upon the wound to produce a thin layer, when the powder is lightly pressed upon the wound by means of a tampon. It adheres to the wound areas alone, and is best removed from the surrounding parts, and particularly from parts that have already become covered with epithelium, by using a tampon or by gently blowing upon the powder. The dressing must be changed as often as necessary during the first days in which discharge is fairly abundant. The author changed the dressing every 2 days at first, later every 3 to 4 days.

In place of the ipecacuanha treatment of dysentery in children, L. Revillet recommends enemata of silver nitrate solution combined with the internal administration of calomel. For children up to 5 years of age a solution of 0.05—0.1 gramme ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains) of silver nitrate in 120—150 c. c. (4—5 oz) of boiled distilled water is used. To it are added 1 to 4 drops of tincture of opium; for older children a solution of 0.1—0.15 gramme ( $1\frac{1}{2}$ — $2\frac{1}{3}$  grains) of silver nitrate in 150—250 c. c. (5— $8\frac{1}{3}$  oz) of water is used, with 4 to 8 drops of tincture of opium. The very first injection immediately produces considerable relief from the trouble. One or two injections are given daily according to the severity of the case, and the treatment is continued for 2 to 3 days until the symptoms leave off; the treatment is renewed whenever the symptoms recur. The night following the first injection the child is given 0.15—0.3 gramme ( $2\frac{1}{3}$ —5 grains) of calomel according to its age, and a second dose of calomel is given if necessary, after 48 to 72 hours.

Revillet, La clinique infantile 1910, October 1. — Revue de thérapeutique 1910, p. 790.

For the treatment of ulcers of the leg Schaffer recommends silver nitrate in the form of ointments and solutions to stimulate the ulcers. The prescription for his "black ointment" is as follows:

Rp. Argent. nitr.	0.03—0.1—0.3 gramme ( $\frac{1}{2}$ — $1\frac{1}{2}$ —5 grains)
Balsam. Peruv.	1.5—3.0 grammes (24—48 grains)
Zinc. oxid.	3.0 grammes (48 grains)
Vaselin. flav. ad	30.0 grammes (1 oz)

If the weaker ointment produces no inflammation the stronger ointment is used, and the strength may be increased even to 2 p.c. of silver nitrate and 20 p.c. of Balsam of Peru. If the formation of granulations does not proceed as rapidly as desirable in spite of prolonged treatment with the ointment, the ulcer may be touched with a stick of lunar caustic or the base of the ulcer may be cleansed with a solution of 2 grammes (30 grains) of silver nitrate in 20 grammes ( $\frac{2}{3}$  oz) of 60 p.c. alcohol.

### Argentum colloïdale.

Recent reports of Riehl have shown collargol to be of good service in ascites, in which it has enabled him to dispense with tapping which frequently very considerably weakens the patient. Riehl used the so called "Unguentum Credé", 3—4 grammes of which were applied by inunction for 15 to 20 minutes into the skin of the abdomen or of the back, after the skin had been thoroughly cleansed in an ordinary bath or in a Turkish bath; the applications were usually made every 3 or 4 days. After treatment the part was covered with wool and Billroth's battist. In 3 cases described by the author this treatment led to a great diminution of the ascites after a short time, and a considerable coincident increase in the quantity of urine. The result is undoubtedly due to an irritant action of the silver upon the renal epithelium, and is due to an increased activity of the kidneys. An increase in diuresis produced by collargol has recently been described by H. Albrecht who has written an interesting paper describing the value of the prepa-

Schaffer, Beihefte zur Medizinischen Klinik 1910, No. 5, p. 150.

Riehl, Münchener medizinische Wochenschrift 1910, No. 21, p. 1120.

Albrecht, Münchener medizinische Wochenschrift 1909, No. 51, p. 2621.

tion in puerperal sepsis and other septic diseases. He came to the conclusion that collargol is entirely useless when given intravenously in the treatment of general infections and severe local suppuration. Its action is prompt, however, in severe intoxication having the features of a septic general infection. Its action is not antibacterial and is not due to any power of exciting leucocytosis; it has a catalytic effect consisting in a successful absorption and increased oxidation, thereby rendering the toxins harmless. D. Popow also obtained very satisfactory results with collargol, used subcutaneously, in puerperal affections.

Th. Gramenitzki prescribed collargol in the form of intra-urethral injections in obstinate cystitis, in tuberculosis of the bladder and in hæmorrhage due to tumours of the bladder and prostate. The bladder is first washed out with a 3 p. c. solution of boric acid. He then injects 50 to 100 c. c. ( $1\frac{2}{3}$ — $3\frac{1}{3}$  oz.) of a 1 p. c. solution of collargol, and the patient retains this until severe straining to pass water is set up. This treatment proved successful in every case.

F. Daxenberger has published a paper on the use of collargol in ophthalmic practice. In a case of *ulcus serpens corneæ* in which the cornea was half destroyed and the anterior chamber was almost completely filled by a hypopyon, he cleansed the eye and then instilled atropine, followed by the application of a large amount of a 2 p. c. collargol solution. The dressing was only changed once a day. Suppuration ceased during the following days, the ulcer became smaller and cleaner, the exudation was absorbed and the remaining corneal opacity cleared up under dionin treatment. In very severe cases of *ulcus corneæ* the author recommends the instillation of collargol 2 to 3 times a day, and the application of a hollow dressing, while collargol ointment is rubbed in at the temple or the back of the neck. Collargol treatment was also found by Daxenberger of use in *ophthalmia neonatorum*, *dacryo-cystitis*, *blepharo-conjunctivitis*, *blepharitis*, *trachoma*, etc.

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Popow, *Wratschebnaja Gazeta* 1909, No. 31.

Gramenitzki, *Russkij Wratsch* 1909, No. 44.

Daxenberger, *Wochenschrift für Therapie und Hygiene des Auges* 1910, No. 36, p. 293.



Internally Brener has used collargol for the treatment of pneumonia and broncho-pneumonia. Adults were given 0.05 gramme ( $\frac{3}{4}$  grain) 3 times a day in pills, children the following mixture:

Rp. Collargol	0.02—0.06 gramme ( $\frac{1}{3}$ —1 grain)
Glycerin.	20.0 grammes ( $\frac{2}{3}$ oz)
Aq. destill.	30.0 grammes (1 oz)

M. Sig.: To be given in tablespoonfuls during the course of a day.

For children the author gives 0.01 gramme ( $\frac{1}{6}$  grain) as the daily dose for every year of the child's age. The results obtained by this treatment are described by Brener as very satisfactory.

An excellent result from the internal use of collargol has been described by Kucera. In a case of tuberculous mixed infection, in which the sputum contained streptococci and Fränkel's diplococci in addition to tubercle bacilli, he gave collargol in combination with sulphurated antimony, sodium bicarbonate and dionin or codeine. At first he gave 3 powders a day and gradually increased the amount to 8 powders a day (each containing 0.02 gramme [ $\frac{1}{3}$  grain]). This treatment was followed by a surprisingly good result. After 6 days the night sweats had left off, after 8 more the patient was free from fever, had a good appetite and was able to spend the day in the garden, and this was not the case before the use of collargol. After 5 weeks' treatment no bacteria, not even tubercle bacilli, could be found. Other trials with collargol were equally successful in cases of tuberculous mixed infection of the lungs in young rapidly growing persons.

### Argyrol.

Stadtfeld prefers argyrol to silver nitrate in the treatment of ophthalmia neonatorum, but van Lint was

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Brener, *La Pédiatrie pratique* 1910, March 25. — *Revue internationale de médecine* 1910, No. 14, p. 303.

Kucera, *Allgemeine militärärztliche Zeitung* 1910, No. 2. — *Deutsche Medizinal-Zeitung* 1910, No. 37, p. 663.

Stadtfeld, *Hospitalstidende* 1909, No. 16. — See Merck's Reports 1909, p. 119.

van Lint, *La polyclinique* 1910, June 15. — *Revue internationale de médecine* 1910, p. 322. — *La clinique ophtalmologique* 1910, September 10.

led by his trials to an opposite view. He admits the value of argyrol, however, in the treatment of acute and subacute conjunctivitis, in phlyctenules, and, in combination with zinc sulphate, in corneal ulcers. He obtained good results, too, by the preventive use of argyrol in measles which is often accompanied with conjunctivitis and keratitis. He used a freshly prepared solution (0.5:5.0) and instilled one drop every two hours. Stronger solutions are not regarded by the author as of use, but if energetic treatment is required he recommends its more frequent use, while in less severe cases 2 to 3 instillations are said to suffice. The author lays particular value on the mode of preparation of the argyrol solution, for a solution properly prepared produces a pleasant sensation, while one improperly prepared gives rise to pain. The former, when prepared at ordinary temperature, is said to have the colour of tincture of iodine, and to be particularly suitable for children because of its freedom from irritant properties. Argyria is not to be feared if we may judge by the experience of van Lint, provided the treatment with argyrol is not continued for longer than 6 months. If it is necessary to prolong the treatment still further, another remedy should be employed. The safest plan is to change the remedy after 2 to 3 months.

### **Aristochin.**

The advantages of this tasteless quinine derivative in children's practice are extolled by D. Lévai. He draws particular attention to the value of the remedy in typhoid fever. In his opinion it is never so appropriate as in this case, for most antipyretics injure the heart and cannot be used without great care. Aristochin, however, may be used without fear of this contingency, at any rate the author has used it in more than 100 cases without any apparent injury. It was always found useful, even though it did not abbreviate the duration of the illness. At any rate, it renders the disease more tolerable both to the patients and to those in charge of them. Although typhoid fever does not run an afebrile course under systematic aristochin treatment, still the typhoid state is less marked than usual,

there is less apathy and somnolence, and the other nervous manifestations are less severe. This renders it easier to nourish the patient, and is of considerable value in the whole course of the illness. The author considers aristochin to be the most suitable quinine preparation for children in other indications such as pertussis, for no unpleasant secondary effects occur as is the case with quinine, even when administered in large doses.

### **Arsacetin.**

This preparation, introduced into therapeutics by Ehrlich, has been made the subject of varied reports during the past year. It appears certain now that it cannot be regarded as a comparatively harmless substance, though the first publications made it out to be so. Its therapeutic value as an antisyphilitic is not affected by this circumstance. Further study of its dosage and contra-indications are required to furnish more definite data. Thus Pflughöft, who gave small doses of arsacetin for a long period in a case he describes, believes that with careful observation of the eyes, and with small doses, it is possible to detect the presence of unusual sensitiveness on the part of the patients sufficiently early to prevent permanent injury, by discontinuing the treatment in time. F. Jenssen, however, believes that there is no way of avoiding serious injury to the sight by the use of arsacetin in individual cases, and for this reason it should only be used in very special cases in which all other remedies have proved of no avail, and even then it should be used with great caution. Further, he regards the various forms of mercurial treatment as superior to arsacetin. The author admits that syphilitic symptoms may be relieved by arsacetin, that its curative effect is particularly noticeable in severe affections of the skin and nails, and in swelling of the glands, and that its use is frequently followed by the conversion of a positive Wassermann's reaction to a negative one. It must be assumed further, that in primary syphilis there are but few isolated cases in which an immediate complete cure is obtained by

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Pflughöft, *Münchener medizinische Wochenschrift* 1910, No. 26, p. 1395.

Jenssen, *Dermatologische Zeitschrift* 1910, No. 4.



its use. In fact, with arsacetin treatment the secondary symptoms occur somewhat earlier than is the case following a course of mercury. In secondary and tertiary syphilis it is said that the preparation does no permanent good. S. Sowade comes to the following conclusions: In his experience, though arsacetin relieves syphilitic symptoms, especially tertiary and malignant symptoms, it is not able to prevent relapses, and its action as a rule is less trustworthy and less enduring than that of mercury. G. Meszczersky's opinion is even less favourable. He found the action of arsacetin very irregular in recent cases of syphilis. In one case it would have a prompt action, in another its action would fail entirely. Moreover, the remedy is very poisonous and it is impossible to carry out systematic treatment with small doses, for it is impossible to calculate in advance its toxic action on the kidneys.

O. Neugebauer tried to improve the action of arsacetin by combining its use with the administration of mercury and quinine. The patients were given an intramuscular injection every week consisting of 1 c.c. of a 10 p.c. emulsion of salicylate of mercury followed on the next day by an injection of 1 c.c. of arsacetin solution (10 p.c.), repeating the arsacetin injection on the third day, and giving by mouth three times a day 0.5 grammè ( $7\frac{1}{2}$  grains) of bisulphate of quinine, if the patients stood it well. The result of this combined treatment was not satisfactory. Naegeli on the contrary reports excellent results from the use of arsacetin in pseudo-leukæmic glandular affections. A man of 40 had an illness with continuous high, though somewhat irregular fever, leading to increasing cachexia, and threatening to end fatally. Abscess of the liver was suspected, and an exploratory laparotomy was performed when extensive retroperitoneal glandular swellings were discovered. Arsacetin was given internally (0.05 grammè [ $\frac{3}{4}$  grain] 4 times a day) whereupon the fever, which had persisted at a high level for 7 months, subsided and after 2 days disappeared completely, his condition improving rapidly and continuously. He gained 31 lb. in weight, and made a complete recovery. In two other

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Sowade, Archiv für Dermatologie und Syphilis 1910, No. 1.

Meszczersky, Wratschebnaja Gazeta 1909, No. 27.

Neugebauer, Wiener klinische Wochenschrift 1910, No. 4, p. 128.

Naegeli, Therapeutische Monatshefte 1910, No. 2, p. 58.

cases arsacetin had a strikingly good action. Excellent results were also obtained by M. Kranzfeld and by K. Georgiewski and S. Nomikosow in recurrent fever. Small quantities injected daily were not found to yield satisfactory effects, while doses of 0.6 gramme (9 grains) (at intervals of 4 to 6 days) had an excellent action.

With regard to the value of arsacetin in trypanosomiasis, it appears to be less efficacious than atoxyl. This, at any rate, is Eckard's opinion. He was unable, after his trials, to agree with Ehrlich's view that arsacetin is less poisonous than atoxyl, while in larger doses it is equally efficacious. He considers atoxyl to be still the best remedy for sleeping sickness.

The secondary effects of arsacetin and the way of avoiding them have been specially studied by H. Oppenheim, F. Hammes, H. Borchers and I. Iversen. Oppenheim and Hammes report two cases in which blindness occurred after comparatively small doses of arsacetin. In one of these cases 0.1 gramme ( $1\frac{1}{2}$  grains) had been injected every 2 days, or 1.8 grammes (28 grains) in all during 6 weeks. In the other case doses of 0.1 gramme ( $1\frac{1}{2}$  grains) had been given every 2 days and the untoward result had occurred after the eighth dose. Iversen considers that the harmful effect of arsacetin on the optic nerve has not yet been explained, and he looks for an explanation in personal idiosyncrasy. The author considers that the greatest possible care is required in cases of abuse of alcohol, of excessive smoking and where other arsenic preparations have already been used. Other symptoms such as colic, hæmorrhage into the sclera, scarlatinal erythema, etc., are to be taken as warnings of the presence of hyper-sensitiveness. Borchers made a special study of arsacetin in relation to its

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Kranzfeld, *Therapeutischeskij Oboshrenie* 1909, No. 13.

Georgiewski-Nomikosow, *Charkowski medizinkoje Journal* 1910, Vol. 6, No. 5.

Eckard, *Archiv für Tropenhygiene*, Vol. 14, No. 2. — *Medizinische Klinik* 1910, No. 20, p. 797.

Oppenheim, *Berliner klinische Wochenschrift* 1910, No. 5.

Hammes, *Deutsche medizinische Wochenschrift* 1910, No. 6, p. 267.

Borchers, *Dissertation Jena* 1910. — *Münchener medizinische Wochenschrift* 1910, No. 8, p. 408.

Iversen, *Russkij Wratsch* 1909, No. 49. — *Petersburger medizinische Wochenschrift* 1910, No. 30, p. 402.

irritant properties on the kidneys. He found the latter to be more pronounced than in atoxyl. In 10 cases of syphilis in which the author injected arsacetin inflammation of the kidneys appeared in every case, and in 5 cases it was so severe that the treatment had to be left off. On the other hand the author has never observed injury to the eyes, although he gave fairly large doses (0.4—0.6 gramme [6 to 9 grains]). The remedy had a rapid and favourable action on the later manifestations of the secondary stage and in the third stage.

The internal use of arsacetin appears to be unattended with danger, and fairly efficacious. Heinrich places the dosage at 5 to 8 drops of a 10 p.c. solution 3 times a day, and obtained very good results in pseudo-leukæmic tumours, diabetes insipidus due to tuberculosis, psoriasis and lichen ruber. The author therefore recommends further trials with the internal administration of arsacetin in small doses.

### **Arsenophenylglycin.**

In a report on the treatment of sleeping sickness in Togo, Zupitza and v. Raven report their results with the use of arsenophenylglycin. This preparation was found to give better results than atoxyl although the latter gave good results if applied in time. The idea of curing the patient by a single application or by a double injection, however, was doomed to disappointment. Further, the duration of the action has not yet been determined with certainty, for the duration of freedom from parasites following an injection is subject to considerable variations. Like atoxyl and arsacetin, arsenophenylglycin has also produced serious toxic symptoms, and in two cases the authors believe the preparation to have been responsible for the fatal termination. A specially striking result obtained by the authors is the fact that toxic symptoms are produced, not by a single large dose, but by giving repeated doses at short intervals. A double injection within two days is said to be free from danger, while the same dose divided into 4 or 6 amounts given within 10 to 15 days may produce serious disturbances.

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Heinrich, *Therapeutische Monatshefte* 1910, No. 11, p. 593.

Zupitza - Raven, *Berliner klinische Wochenschrift* 1910, No. 33, p. 1561.



For this reason the authors consider that advanced cases of sleeping sickness should not be treated with arsenophenylglycin, for in such cases it would be necessary to repeat the injections a number of times. In recent cases, on the other hand, we may give large doses, 0·8 to 1 gramme (12—15 grains) on one day or on two consecutive days. Should a relapse occur within 6 weeks other remedies must be used, and arsenophenylglycin must not be used again under 8 weeks.

Miessner obtained a surprising cure in a mare suffering from chronic heat by two injections of arsenophenylglycin. Fröhner tried it in a stallion suffering from the same complaint. He gave the animal 24 grammes (360 grains) of arsenophenylglycin (in 1·5 litres [52 oz] of normal saline solution) intravenously. This was shortly followed by psychic excitation and severe colic, and on the following day by inflammation of the kidneys. Further, a large wheal formed. As for the disease no improvement was perceptible during the nine months following the injection. On the contrary, the condition continued to become considerably worse. A second injection given seven months later was again followed by no benefit. All the same the author considers further trials should be made, particularly in acute cases.

### **Arsentriferrin.**

A. Teubert tried this preparation\*) in anæmic conditions, especially those following severe illnesses, in chlorosis, neurasthenia and nervous debility or weakness, in hysteria, scrofulous affections and skin diseases. In all cases he used arsentriferrin in tablets of 0·3 gramme (5 grains), children were given 1 to 3, adults 3 to 5 tablets, after food. After 14 days' treatment he allowed an interval of 8 days, when he commenced the treatment anew. The duration of treatment varied, according to the nature of the disease, from 5 to 12 weeks. By giving it in the above described manner it was possible to use triferrin in chlorosis, even in severe cases with troublesome subjective gastric symptoms, in cases where hæmatogen, ferro-manganese

Mießner, Berliner tierärztliche Wochenschrift 1909, No. 34, p. 634.

Fröhner, Berliner tierärztliche Wochenschrift 1910, No. 23, p. 461.

Teubert, Berliner klinische Wochenschrift 1910, No. 28, p. 1349.

\*) See Merck's Index 1910, p. 48.

solution and Blaud's pills frequently caused pain and vomiting after a few days, he was able to continue the treatment for weeks without the occurrence of troublesome secondary effects in the stomach and intestine. A further advantage is the fact that children from 3 to 6 years of age take the remedy readily. As regards the mode of action of arsen-triferrin, the author was able to observe that in all cases it produced a more or less considerable gain in weight. This was apparent in a number of convalescents recovering from severe diseases, such as influenza and other infective diseases, in which the use of the remedy was followed by a surprisingly rapid improvement in the general condition of strength. Similar results were obtained even in advanced cases of pulmonary tuberculosis, although the good effects were transitory. In skin diseases arsen-triferrin is also of good service as an auxiliary to the specific treatment. The author finds it of especial value in itching diseases of the skin and in scrofulous affections involving the lymphatic apparatus. In these cases the glandular swelling and other unpleasant symptoms appear to subside more rapidly under the action of the drug. The best results were obtained by Teubert in nervous diseases in which there were no demonstrable severe pathological changes in the nervous system, as for example in chorea minor, neurasthenia and hysteria, and also in hysterical affections of children. He attributes his good results to the very suitable composition of arsen-triferrin.

### Asurol.

The therapeutic results obtained with asurol\*) have been reported on during the past year by K. F. Hoffmann, E. Bäumer, Fr. v. Veress and H. Rock. Hoffmann found asurol preferable to calomel and salicylate of mercury in the treatment of syphilis, for being soluble in water it diffuses throughout the organism far more readily than the above named salts of mercury. The author injected 2 c. c. (34 min.) of a 5 p. c. solution every 2 days until

\*) See Merck's Reports 1909.

Hoffmann, Medizinische Klinik 1910, No. 27.

Bäumer, Berliner Klinik 1910, No. 264.

Veress, Heilkunde 1910, No. 8.

Rock, Wiener klinische Wochenschrift 1910, No. 33.

the syphilitic symptoms disappeared. The action of the preparation is said to be striking, and such as can only be obtained by calomel, certainly not by inunction. In proof of this we have the rapid cure of psoriasiform exanthemata within nine days. In primary affections a difference was observed in its action, readily accessible ulcers usually healed completely on the fourth day, after 2 injections coupled with simultaneous local treatment, while primary affections at the urethral orifice and deep in the sulcus coronarius required 4 to 6 injections, and did not disappear until after 10 to 12 days. In broad condylomata, maculous rashes and papular eruptions on the tonsils, asurol exerted a fairly rapid action. It is soluble and is quickly excreted by the organism; Hoffmann therefore completed his cures by the use of grey oil, whereby the effect of asurol is considerably enhanced. The author was also able to ascertain that asurol led to increased leucocytosis. However, the preparation like nearly all other remedies, is not free from unpleasant secondary effects. In many cases it causes pain of varying severity at the seat of the injection, and the pain sometimes extends along the legs, and it was not possible to diminish the pain by the addition of anæsthetics to the asurol. The author points out, however, that the asurol injections never produced infiltration. Further, the kidneys are never injured by the treatment and the gums are scarcely ever affected. More unpleasant effects than these local pains was the occurrence of colic, but this occurred in 5 p.c. only of the cases treated. Bäumer also obtained satisfactory results. He found it best to commence asurol treatment with intramuscular injections of 0.5 to 1 c.c. (8—17 min.) of a 5 p.c. solution, subsequently gradually increasing the doses to 2 c.c. (34 min.), and with constant examination of the urine. 12 to 15 injections at intervals of four days were found to be sufficient. He also observed the occurrence of colic or slight diarrhoea now and then, but no albuminuria. The action of asurol was always found to be prompt and certain. In a later publication\*) Bäumer states that he now always uses the 10 p.c. asurol solution so as to prevent relapses. For the first injection he gives 3 divisions of a syringe of 2 c.c. capacity. This is followed, after 3 to

\*) Bäumer, Therapie der Gegenwart 1910, No. 10, p. 479.



4 days, by 5 divisions, and he uses in all at least 15 injections. The result of this treatment is said to be satisfactory, although it may not be as permanent as that obtained from the use of insoluble solutions of mercury.

Rock found that asurol accelerated the subsidence of syphilitic manifestations though its action is not enduring. The secondary effects usually disappear at once on discontinuing the use of the remedy, and no disturbances of long duration are produced by it.

### Atoxyl.

F. Mendel tried atoxyl in a case of Graves's disease which had resisted other forms of treatment, and he obtained a certain amount of success. After several weeks of intravenous atoxyl injections in increasing doses the author observed a slight improvement in the general condition, though the objective symptoms showed no improvement until a combination of atoxyl with sodium iodide was used in the form of intravenous injections. After the first of these injections the tremors stopped and the goitre began to diminish in size. The exophthalmos, however, was not improved. The general condition showed a striking improvement which was especially apparent in an increase in appetite, a better frame of mind and a considerable gain in weight. After 20 injections the pulse-rate had dropped from 140 to 90. Mendel obtained equally good results in a number of other cases of Graves's disease. He therefore recommends for injection a dose of 2 c.c. (34 min.) of the following solution:

Rp. Atoxyl	1.0 gramme (15 grains)
Sod. iodid.	4.0 grammes (60 grains)
Aq. destill. ad	20 c.c. ( $\frac{2}{3}$ oz)

Each dose contains 0.1 gramme ( $1\frac{1}{2}$  grains) of atoxyl and 0.4 gramme (6 grains) of sodium iodide. It is given every day or every other day according to the severity of the disease, and as improvement becomes apparent, one or two injections are given weekly. The solution is also issued ready for use in ampoules under the name of "Iodarsyl".

The communications of R. A. Lundie and R. H. Blaikie show that atoxyl is apparently of good service in pul-

Mendel, *Therapie der Gegenwart* 1910, No. 2.

Lundie-Blaikie, *Berliner klinische Wochenschrift* 1910, No. 9.

monary tuberculosis, and this is no wonder, for sodium cacodylate\*) had been used for many years with some success in the treatment of tuberculosis. The authors' treatment consists in giving the patient on two consecutive days an injection of 0.6 gramme (9 grains) of atoxyl, the application of the remedy being then discontinued for 14 days. With this treatment the authors observed the occurrence of slight toxic symptoms in one case only, while about two-thirds of the patients complained of local pain. Even in advanced cases they obtained an improvement in the general condition and a rapid cessation of the cough and expectoration. In two cases the improvement was of long duration (13 months) but some of the patients derived little or no benefit from the treatment.

In recurrent fever S. Jarussow formed a favourable opinion of the action of atoxyl in most cases. He found that the remedy cuts short the illness, which frequently remains limited to the first attack, or failing this the second and third attacks are abbreviated, while there is a diminution in the number of spirochætæ and a prolongation of the first period of apyrexia, and in other respects the illness runs a less severe course and there are fewer fatal cases.

On the use of atoxyl in syphilis we have the reports of P. Villanova, E. Welander, J. Peyri and H. Sowade. Welander prescribed the remedy with varying results in doses of 0.4 to 0.75 gramme (6—11 grains) every 2 to 3 days. Of more interest are his observations on the elimination of the preparation by the organism. It appears that atoxyl undergoes no chemical change in the organism and is eliminated unchanged. This shows that the remedy acts as such and does not require to be changed into arsenic acid or arsenious acid, to enable it to act. The author also found that the excretion of atoxyl takes place to a very large extent in the urine, while only a small quantity is passed with the fæces. Within the first 24 hours after

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\*) See the article "The Cacodylates and their Therapeutic Uses", p. 1.

Jarussow, *Medizinskoe Oboshrenie* 1909, No. 12.

Villanova, *Revista de medicina y cirugía* 1910, No. 8.

Welander, *Hygica* 1909, p. 97.

Peyri, *Revista de medicina y cirugía* 1910, No. 8.

Sowade, *Archiv für Dermatologie* 1910, No. 1.

the injection about 60 p.c. of the atoxyl is eliminated, while the remainder requires more than 3 weeks for its excretion. This explains in part the need for exercising great care in using the preparation if its ill-effects are to be avoided. Sowade, Villanova and Peyri consider that the remedy should not be used for fear of these ill-effects, although they are not able to deny its good effect in syphilis. A similar view was expressed by A. Birch-Hirschfeld who observed the occurrence of complete blindness in 2 patients in whom he had given atoxyl injections for the treatment of psoriasis. One of them had been given 32 injections, or 3 grammes (45 grains), in all, the other 45 injections, or 6.4 grammes (96 grains). K. Muto pointed out further that the use of atoxyl in various animals might cause hæmorrhage in the kidneys, heart and small intestine. The case described by J. de Azù a of blindness after the injection of 21 grammes (315 grains) within 33 days can only be attributed to the excessive doses of atoxyl used\*).

Atoxyl appears to be of more value in veterinary practice, Bochberg found that horses could stand large doses amounting to 1.75 grammes (27 grains) without harm. In treating inflammation of the chest he began with injections of 0.3 gramme in 10 grammes (5 grains in  $\frac{1}{3}$  oz) of water, and increased the dose daily up to 0.75 gramme (11 grains) without observing any secondary action. With the ordinary symptomatic treatment the general condition of the horses remained below par for a long time, but with atoxyl treatment the contrary was the case. After a few days the desire for food returned, even in horses which were very ill, the temperature fell and the pulse-rate diminished. After 10 to 14 days the animals as a rule appeared perfectly healthy, and after 2 to 4 weeks they were able to return to work. The author therefore recommends the further use of atoxyl.

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Birch-Hirschfeld, Fortschritte der Medizin 1910, No. 30.

Muto, Archiv für experimentelle Pathologie und Pharmakologie 1910, Vol. 62, No. 6.

de Azù a, Rivista clinica de Madrid 1910, No. 1.

\*) See also: K. Steindorff, Die Wirkung des Atoxyls auf das Auge. Berliner klinische Wochenschrift 1910, No. 40.

Bochberg, Zeitschrift für Veterinärkunde 1910, No. 7.



W. Dietrich has carefully studied the dosage of atoxyl in dogs and horses. He comes to the following conclusions: In dogs a subcutaneous dose of 0.01 gramme per kilogramme has little poisonous action, while a dose of 0.02 gramme is fatal. Repeated doses of 0.005 gramme per kilogramme produce a fatal result after 6 days, when given every day, and after 6 weeks or so when given twice a week. Smaller doses, when continued for a long time, may give rise to chronic intoxication. The dose for daily administration varies according to the size of the dog between 0.01 to 0.2 gramme, for long continued use 0.001—0.02 gramme. In horses a subcutaneous dose of 0.04 gramme per kilogramme of horse has a toxic action, and so have repeated daily doses of 0.007—0.01 gramme. The single dose for horses is 5 to 10 gramme (75—150 grains) according to their weight, for prolonged daily use 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains). Continued daily doses in excess of these may give rise to blindness and deafness in the animals.

### **Atoxylic mercury.**

In a comprehensive paper Uhlenhuth and Mulzer describe the results of their experimental study of the value of atoxylic mercury\*), and discuss the results that are to be expected from the use of this remedy. It showed a good effect in syphilis in rabbits, and the results in man appear to have been equally favourable. Hence it may be expected to take a permanent place in the therapeutic treatment of syphilis. A decisive opinion cannot be uttered, however, until it has been used for years.

Atoxylic mercury is warmly recommended in a paper by O. Boethke, in which he shows it to be a useful remedy. The cases that react best to the remedy are recent cases of syphilis, and then those with primary and secondary manifestations. The most resistant are tertiary cases, with the exception of ulcerations of the gums. With regard to the occurrence of secondary effects the author

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Dietrich, Deutsche tierärztliche Wochenschrift 1910, No. 6. —

Berliner tierärztliche Wochenschrift 1910, No. 23.

Uhlenhuth-Mulzer, Deutsche medizinische Wochenschrift 1910, No. 27, p. 1262.

\*) See Merck's Reports 1909.

Boethke, Medizinische Klinik 1910, No. 15, p. 578.

observed neither retinal hæmorrhage nor optic nerve atrophy to follow its use, while in 2 cases only were there traces of albumin in the urine. On the other hand pain and infiltration at the seat of the injection occur now and then, while more rarely there was a rise of temperature with pain in the head and chest, and in one case only did colic and severe stomatitis occur. The best method of administration is by injecting 0.1 gramme ( $1\frac{1}{2}$  grains) into the gluteal region once a week. This method is more convenient and cleaner than treatment by inunction. It does not require to be frequently repeated, and only a small total quantity of mercury is necessary for a cure.

F. J. Lambkin is also well satisfied with the action of atoxylic mercury. He gave 8 injections in the course of a month, giving as much as 0.1 gramme ( $1\frac{1}{2}$  grains) in olive oil or liquid paraffin for a dose, and he occasionally added creosote, camphoric acid and palmitin. He observed a rapid disappearance of the symptoms. The injections gave rise to no unpleasant secondary symptoms, and those containing creosote did not cause pain.

R. Bergrath in his trials came to the conclusion that atoxylic mercury had no advantage over other mercurial preparations in the treatment of syphilis in man, while its action was not nearly as good as that of other remedies. The good results obtained by Uhlenhuth in animal experiments could not be applied without further enquiry to the human pathology of syphilis. Uhlenhuth, in his animal experiments, used doses which were comparatively high, as much as 0.05 gramme per kilogramme of rabbit. In the case of man the enormous dose of 1 gramme (15 grains) would be necessary to obtain the same result. With the far smaller doses that have hitherto been used the preparation therefore gives poor results.

### **Atropinæ sulphas.**

Atropine has been repeatedly recommended for the relief of intestinal obstruction in paralytic ileus. A. Lederer, in cases in which a certain diagnosis could be made, used it

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Lambkin, *Lancet* 1910, No. 4505, p. 23.

Bergrath, *Deutsche medizinische Wochenschrift* 1910, No. 37, p. 1694.

Lederer, *Medizinische Klinik* 1910, No. 1, p. 11.

with very satisfactory results. As a rule he gave a subcutaneous trial dose of 0.001 gramme ( $\frac{1}{64}$  grain) and then a larger dose of 0.003 to 0.005 gramme ( $\frac{1}{20}$ — $\frac{1}{12}$  grain) of atropine sulphate. In one case only the action was delayed for more than ten hours. The injection treatment was supported by enemata which did not prove effective, however, until the drug had been given. In 2 cases the occurrence of severe toxic symptoms were observed, consisting of delirium with great restlessness, thirst and burning pain in the throat. These symptoms soon subsided without special treatment. After checking the intestinal obstruction, diarrhoea frequently set in and continued for a few days, but then left off spontaneously.

C. Schindler regards atropine as a good auxiliary in the treatment of gonorrhoea. In his view a complication frequently occurs in man, due to the automatic movements in the sexual organs, particularly of the seminal tubules and the seminal vesicles, which are produced independently of the central nervous system, through their peripheral centre, the plexus hypogastricus. This leads to the ascent of the gonococci which are themselves non-motile. For this reason he not only uses local treatment (with protargol) but also atropinises the muscles of the sexual apparatus supplied by the hypogastric plexus, thus checking these movements. For this purpose every patient is given 0.001 gramme ( $\frac{1}{64}$  grain) of atropine sulphate twice a day, or 0.00075 gramme ( $\frac{1}{90}$  grain) 3 times a day from the first day of treatment before complications have set in, and if swelling of the prostate is present, he adds 0.1—0.25 gramme ( $\frac{1}{2}$  to 4 grains) of potassium iodide, applied in the form of suppositories. In using protargol solution for injection into the posterior part of the urethra it is advisable to add 1 c.c. (17 min.) of a 0.1 p.c. solution of atropine sulphate, for it is thus possible to atropinise the colliculus seminalis and the prostate more effectually than from the rectum. This atropine treatment may be continued for weeks. The advantages of the method are confirmed by Genty. Erdős

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Schindler, *Berliner klinische Wochenschrift* 1909, No. 37. — See *Medizinische Klinik* 1910, No. 4, p. 154.

Genty, *La Clinique* 1910, 25<sup>th</sup> July. — *Revue de thérapeutique* 1910, p. 607.

Erdős, *Pester medizinisch-chirurgische Presse* 1910, No. 15.



has also used atropine with success. He found it necessary to give doses of 0.0006 gramme ( $\frac{1}{100}$  grain) 3 times a day. The author first cautiously used smaller doses, and found them insufficient. In cases with very profuse discharge, however, the results of the administration of atropine were not satisfactory.

Just as Schindler sought to set the colliculus seminalis at rest by atropine, so atropine has been used for a considerable time in gastric ulcer to diminish the excitability of the gastric muscles. In this case, however, atropine has a further object, viz., that of reducing the secretion of hydrochloric acid. The atropine treatment of gastric ulcer has recently been described again by K. Schick who recommends its more extensive use. The treatment consists in the daily subcutaneous administration of 0.001 gramme ( $\frac{1}{64}$  grain) of atropine sulphate continued for days or for weeks. Of course this treatment must be supported by dietetic and physical measures.

Atropine sulphate was found by W. F. Waugh to have a hæmostatic action when given in large toxic doses which may be made use of in placenta prævia, post partum hæmorrhage, menorrhagia, metrorrhagia, abortion, epistaxis, hæmoptysis, hæmophilia and in renal hæmorrhage. This action is attributed to an excitation of the vaso-dilators, leading to a fall of arterial pressure, and forcing most of the blood into the capillaries.

### **Benzidine for the detection of blood.**

O. Holmboe has applied Messerschmidt's modified benzidine blood test\*) and the guaiacum test in 75 cases in examining fæces, and found that the benzidine test was more sensitive than the latter in a few cases only. However it has several other advantages over the guaiacum test. It is simple of execution, it is easy to read the result, it saves much time, for it can be carried out in a fraction of the time required for the guaiacum test. Moreover, the benzidine method is cheaper. Holmboe considers the benzidine test

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Schick, Wiener klinische Wochenschrift 1910, No. 34.

Waugh, Medical Record 1909, 27<sup>th</sup> November. — Klinisch-therapeutische Wochenschrift 1910, p. 80.

Holmboe, Norsk Magazin for Lægevidenskaben 1909, No. 12.

\*) See Merck's Reports 1909, p. 140.

to be absolutely accurate, however, as E. Walter has again pointed out, only a negative result may be regarded as an absolutely reliable test. All the same he considers that this test should not be abandoned for this reason alone, as it certainly has great advantages. The benzidine test is certainly adapted to take the place of the guaiacum reaction, a reaction which is still used for the preliminary detection of blood in forensic practice, for if a negative result is obtained there can be no blood present. It is in this very respect that Walter finds the benzidine reaction considerably more trustworthy. His investigations have shown that blood in a dilution of 1:10,000 cannot be detected by the guaiacum reaction, while in a dilution of 1:250,000 the application of the benzidine reaction gives rise to a definite green colour. The author does not recommend the use of benzidine paper, at any rate for forensic purposes. For the detection of blood on objects and on clothing he gives the following directions: The stains suspected of containing blood are well moistened with normal saline solution or with 3 p. c. hydrogen peroxide, while parts that cannot readily be moistened are intimately mixed with the fluid by rubbing with a clean glass rod. After thoroughly moistening the spot it is rubbed with a swab of clean white wool from which all fat has been removed. Upon this swab a few drops of benzidine dissolved in glacial acetic acid (the benzidine is taken up on the point of a knife and dropped into 3 c. c. of glacial acetic acid) are dropped at once, and then a few drops of hydrogen peroxide (3 p. c.) are dropped upon it. If the stain contains blood a green or blue colour appears at once on the swab. The test is so remarkably sensitive that a negative reaction makes the absence of blood certain. In this way it is easy, in examining a number of stains suspected of containing blood, to exclude quickly those that contain none. Another advantage of this method, as described by Walter, is that the clothing is not injured, while the stains are in no way altered for the purpose of subsequent investigation. We cannot substitute filter paper or linen for the wool, for the use of these substances readily gives rise to errors. On the other hand we may substitute for the benzidine solution the tablets recommended last year by Walter, consisting of benzi-

dine and sodium perborate\*), one of these tablets, containing 0.1 gramme, is dissolved in 10 c.c. of glacial acetic acid and the solution applied in the manner described above, without using hydrogen peroxide. If it is desired to detect blood in solution, we have to take account of the degree of dilution. In very dilute solutions, e. g., 1:50,000 to 100,000, a definite green colour is obtained when equal parts of the blood solution and the reagent are mixed together. Both an excess of the glacial acetic acid contained in the reagent, and great dilution of the same by the blood solution interfere with the sensitiveness of the reaction. In less diluted blood solutions a few drops of the reagent are added to 1 c.c. of the blood solution.

F. Bordas uses a method of detecting blood on tissues similar to that of Walter. He soaks the blood stains with water, presses a piece of filter paper upon them — for this purpose the paper must be absolutely free from iron — and then drops upon it benzidine solution and hydrogen peroxide. In this case, again, a negative reaction is the only absolutely trustworthy test. It is advisable to begin by making a blind experiment with the filter paper that is to be used with benzidine and hydrogen peroxide, to make sure that the paper does not give rise to a blue colour without blood.

For the detection of blood in urine J. H. Greef gives the following directions: The urine is well stirred, and 2 c.c. are placed in a test tube and rapidly brought to boiling. This fluid is poured very slowly over the walls of a filter consisting of best filter paper. Upon the paper thus moistened a fresh solution of benzidine (about 3 c.c.) to which 3 to 5 drops of glacial acetic acid and 1 c.c. of hydrogen peroxide have been added, is also slowly poured. If traces of blood or of blood pigment are present, a beautiful blue colour immediately appears on the moistened parts of the paper.

Greef discovered another reaction which may perhaps be of value in certain differential diagnoses. Pus, when completely free from blood, gives the benzidine reaction. After boiling the pus, the addition of benzidine gives rise to a brownish-pink colour. Pus containing blood, even after boil-

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\*) See Merck's Reports 1909, p. 140.

Bordas, Comptes rendus de l'académie des sciences 1910, I., No. 9, p. 562.

Greef, Medizinische Klinik 1910, No. 45.



ing, gives with the benzidine test a green colour which is rapidly followed by a deep violet coloration.

### **Benzinum petrolei.**

Benzin in combination with iodine has been recently suggested for disinfecting the skin before operations\*). The iodine has naturally been regarded as the most important constituent of this combination, while the benzin has been thought of importance merely because of its power of dissolving fat. C. Zatti probably made use of this property of benzin when he made experiments on the use of this preparation by itself or with petroleum for pre-operative sterilisation of the skin. His method is to remove the patient's clothing immediately before the operation, and while the patient is on the operating table, without employing other antiseptic measures, to rub the skin for 1 to 2 minutes with a swab of wool the size of a fist soaked in petroleum, and then to repeat the treatment for half a minute with benzin. In more than 700 operations, including laparotomies, hernial operations and other surgical procedures, this method is said to have given very good results, and the wound is said to have healed by first intention. Zatti found the skin over the field of the operation to be rendered somewhat fatty by the petroleum, and this protects it from infection. The same effect has been obtained with the iodo-benzin solution by the addition of paraffin oil. At any rate, this appears to be preferable to the benzin treatment.

### **Bismuthi subnitras.**

The comprehensive reports of C. Beck and E. G. Beck prove that bismuth subnitrate is not only a useful diagnostic for the X ray investigation of fistulous passages, but also a useful therapeutic remedy in fistulæ and chronic suppuration.

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\*) See Heusner, Merck's Reports 1906, p. 143 and 1909, p. 236. Zatti, Gazzetta degli ospedali e delle cliniche 1910, No. 47.

Beck, Illinois State Medical Journal 1908, April. — Journal of the American Medical Association 1908, 14<sup>th</sup> March; 1909 2<sup>nd</sup> January; 1909, 18<sup>th</sup> December. — Surgery, Gynecology and Obstetrics 1909, August; 1910, February. — Beiträge zur klinischen Chirurgie, Vol. 62, No. 2 and Vol. 65, No. 1. — Münchener medizinische Wochenschrift 1910, No. 33. — See Merck's Reports 1908, p. 148 and 1909, p. 143.

The form recommended by the authors is a bismuth paste consisting of one part of bismuth subnitrate and two parts of white or yellow vaseline. This paste is warmed, and injected into the fistula by a suitable syringe until all branches of the fistula may be presumed to have been filled with the preparation. By repeated applications of the paste Beck obtained a cure in a large percentage of cases of chronic fistulæ due to spondylitis, coxitis, renal tuberculosis, etc., some of which were not amenable to other forms of treatment. The method has been tested by a large number of investigators, including Ochsner, Matsuoka, Dollinger, Vidakowich, Elbe, Ridlon and Blanchard, Nemenow, Brandes, Steimann, Don, Rosenbach, Fourmestiaux and Lessonde, Lippens, Nové-Jossérand and Rendu, Eggenberger, Reich, Bircher, etc. The opinions vary greatly, some having obtained favourable results and cures amounting to 76 p.c. of the cases treated, while others have had little satisfaction from the method, and draw attention to the dangerous secondary effects which occur fairly frequently. On the other hand others obtained some surprisingly good results, and some

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Ochsner, *Zentralblatt für Chirurgie* 1909, p. 1692. — *Annals of Surgery* 1909, July.

Matsuoka, *Deutsche Zeitschrift für Chirurgie* 1909, p. 508. — *Therapie der Gegenwart* 1910, p. 186.

Dollinger, *Zentralblatt für Chirurgie* 1908, p. 1310.

Vidakowich, *Zentralblatt für Chirurgie* 1908, p. 1487.

Elbe, *Deutsche medizinische Wochenschrift* 1910, p. 617.

Ridlon-Blanchard, *Zentralblatt für Chirurgie* 1909, p. 66. — *American Journal of orthopædical Surgery* Vol. 6, No. 1.

Nemenow, *Zentralblatt für Chirurgie* 1909, p. 362.

Brandes, *Medizinische Klinik* 1910, p. 1258.

Steimann, *Münchener medizinische Wochenschrift* 1908, p. 2535.

Don, *British Medical Journal* 1909, I., p. 1481. — *Merck's Reports* 1909, p. 143.

Rosenbach, *Berliner klinische Wochenschrift* 1909, p. 298.

Fourmestiaux-Lessonde, *Archives médico-chirurgicales de Province* 1910, 15<sup>th</sup> June. — *Revue de thérapeutique* 1910, p. 522.

Lippens, *Presse médicale* 1910, p. 614. — *Journal médical de Bruxelles* 1910, 4<sup>th</sup> August.

Nové-Jossérand, Rendu, *Zentralblatt für Chirurgie* 1909, p. 975.

Eggenberger, *Zentralblatt für Chirurgie* 1908, p. 1309 and 1537.

— *Münchener medizinische Wochenschrift* 1908, p. 2398.

Reich, *Beiträge zur klinischen Chirurgie* 1909, p. 184.

Bircher, *Medizinische Klinik* 1910, p. 2024.

entirely negative results. Several fatal cases have occurred and have been attributed by individual authors to the bismuth salt, and such cases certainly do not encourage the use of the method. In any case care should be exercised in using it. E. G. Beck attributes a want of success with the bismuth treatment in most cases to the presence of sequestra, which can be discovered without difficulty by the X ray picture; their removal is then necessary. Moreover, faulty method impairs the results, particularly the exercise of excessive pressure in making the injection. For this reason the paste used should be soft, e. g., well warmed. This will result in its finding its way into all side passages, for if one branch of the fistula is missed this may give rise to renewed infection. Finally, the bismuth subnitrate itself may be to blame for failures, for Dunning found that it underwent hydrolysis in the organism which varied according to the proportion of its components bismuth and nitric acid, its action, however, in Baer's opinion is due to the hydrolysis of the nitric acid. To prevent unpleasant secondary effects of the bismuth paste Beck suggests that unsuitable cases should not be treated in this way. He also recommends preventive measures. Thus the paste should not be left in the cavity in too large a quantity, otherwise too much absorption may take place. Certain symptoms should be looked for, such as a livid colour of the skin, small blue ulcers on the gums, vomiting, headache, albumin and epithelial casts in the urine, etc. If necessary the paste should be washed out by means of warm sterile oil. For this purpose the injected oil is left for 12 to 24 hours in the cavity to enable it to form an emulsion with the paste. This is then removed by aspiration. As a further indication Beck mentions chronic suppuration in the accessory cavities of the nose, inflammation of the middle ear, mastoiditis, fæcal fistulæ following abdominal operations and fistulæ following resection or extirpation of tuberculous kidneys. As contra-indications we have simple tuberculous joint diseases, acute inflammation, as in cellulitis and suppurating sinuses, biliary and pancreatic fistulæ and cavities communicating with the interior of the skull. An improvement in the technique, according to Brandes, consists in the introduction of the bismuth paste by

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Baer, see *Münchener medizinische Wochenschrift* 1910, p.1737.



means of a sterile catheter or rubber drain, as this enables the furthestmost parts of the fistula to be more completely filled. Further experiments are required to ascertain whether the substitution of bismuth carbonate for bismuth subnitrate would lead to a diminution in the unpleasant incidents attending the above described method without impairing the results. If the curative component of bismuth subnitrate is the nitric acid, which is able to undergo hydrolysis as remarked above, the substitution of the carbonate should be followed by no success. All the same Auburg describes very good results from its use in various fistulæ. He used a paste for his injections consisting of 4 parts of bismuth carbonate and 6 parts of vaseline.

The fact that toxic symptoms may be produced by bismuth subnitrate, even when applied externally upon wound surfaces, is apparent from 2 cases published by Windrath. Which component of the preparation is responsible for the symptoms has not been proved to complete satisfaction even now. It is possible that in some instances one, and in some cases the other component is to blame, according to the disposition and susceptibility of the patients, while in some cases both components may contribute. Methæmoglobinæmia is a certain sign of nitrite poisoning, while stomatitis represents metallic poisoning. The latter was the most prominent symptom in the cases reported by Windrath. The fact that the administration of bismuth subnitrate may lead both to bismuth and to nitrite poisoning appears from the communications of O. Schumm and A. Lorey.

### **Bolus alba sterilisata** (Sterilised Kaolin).

The therapeutic use of kaolin\*) (bolus alba) has been made the subject of investigation by various workers during the last

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Auburg, *Klinisch-therapeutische Wochenschrift* 1910, p. 406.

Windrath, *Medizinische Klinik* 1910, p. 742. — *Deutsche Ärzte-Zeitung* 1910, p. 329.

Schumm and Lorey, *Medizinisch-kritische Blätter*, Hamburg 1910, p. 76.

\*) See Stumpf, Langemak, Georgii, Höpfel, Megele, Fischer, Merck's Reports 1899, p. 139. — Stumpf, Aufrecht, Merck's Reports 1905, p. 39. — Cohn, Lübbert, Görner, Merck's Reports 1907, p. 54. — Walther, *Zeitschrift für praktische Ärzte* 1907/08. — Stumpf, Merck's Reports 1908, p. 151. — Levy, *Dissertation* Freiburg 1908. — Schwarz, Stauder, Frey, Nas-

years. A communication by P. Zweifel is of importance. He reported that the use of kaolin as a prophylactic to prevent suppuration in inflammation of the navel\*) led to tetanus in 4 cases. The infection was attributable to the kaolin which had not been sterilised before use. The author therefore utters a warning against the use of non-sterilised kaolin and similar powders, e. g., talc powder. Sterilisation is chiefly necessary for preparations for external use, for tetanus infection from the internal administration of kaolin is only conceivable in the presence of wounds of the mucous membrane. Zweifel, however, demands that sterilised kaolin should be used for internal administration, for it might occasionally contain typhoid or other pathogenic bacteria. "For this reason some form of sterilisation of kaolin whether by dry heat or by steam, should be demanded for medical purposes." (A preparation answering these requirements is issued by me under the name of "Professor Stumpf's sterilised kaolin".)

Recent communications on kaolin treatment have been made by Trumpp and Nassauer. The latter draws attention once more to the dry treatment of vaginal discharge inaugurated by him, and expressed the hope that this method of treatment will also prove of use in intestinal diseases such as rectal ulcers, proctitis and carcinoma. Trumpp has similarly tried the use of kaolin in rhinitis. In recent cases he succeeded by the suitable use of kaolin in checking the most severe catarrh within 24 hours. The nares remained dry and the residual swelling subsided within 1 or 2 days. No other remedy has been found by the author to give such good results. He attributes the action to the desiccating properties of kaolin, thereby drying up the nutrient medium on which the bacteria subsist, and thus rendering it unsuitable for their further growth. The dry kaolin and the discharge form a paste which is expelled when blowing the nose.

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sauer, Küster, Merck's Reports 1909, p. 144. — Staby, Statistische Sanitätsberichte der Marine 1908. — Trembur, Archiv für Schiffs- und Tropenhygiene 1908, p. 389. — Martini and Grothe, Deutsche medizinische Wochenschrift 1910, p. 900. Zweifel, Münchener medizinische Wochenschrift 1910, p. 1787.

\*) See Horn and Galatti, Merck's Reports 1908, p. 152.

Trumpp, Münchener medizinische Wochenschrift 1909, p. 2422. Nassauer, Münchener medizinische Wochenschrift 1910, p. 83.

The most favourable cases for the treatment are those in which the nasal passages are wide, rendering it easy for the kaolin to reach all affected parts of the mucous membrane, for naturally the powder can only act when it can be brought into direct contact with the bacteria. If the swelling is so great as to render this impossible, it must first be reduced by suitable treatment. This may be done by means of an ointment consisting of 0.03 gramme ( $\frac{1}{2}$  grain) of adrenalin or suprarenin, 25 grammes ( $\frac{5}{6}$  oz) of unguentum acidi borici and 5 grammes (90 min.) of paraffinum liquidum. The more recent the case and the less the mucous membrane is affected, the more rapid is the result. The powder is administered by means of an insufflator. We need not lay special stress on following Zweifel's advice in this case and insisting on the use of sterilised kaolin.

With regard to the internal use of kaolin in children's practice, Klotz was able to convince himself that the remedy was harmless, but he was unable to note that it possessed any uncommon action. He was unable to observe that the use of kaolin in diarrhoea in acute disease of nutrition in infants led to a cure more rapidly than following the customary tea diet. In meteorism in infants, again, he observed no particularly striking results. He recommends the external use of kaolin, however, as a dusting powder in intertrigo and in mild forms of moist eczema. In vulvo-vaginitis in infants the external use of kaolin is said to give surprisingly good results.

Stumpf has given the following directions for the internal use of kaolin: To prevent kaolin from caking when stirred up with water it is strewn upon double the quantity of water and left to sink to the bottom of its own accord. It is then thoroughly stirred. In enteritis with unobstructed intestinal passages, even in severe cases, adults are given 200 to 300 grammes ( $6\frac{2}{3}$ —10 oz) of kaolin suspended as described. Infants may be given 25 to 30 grammes ( $\frac{5}{6}$  to 1 oz) and 10 grammes ( $\frac{1}{3}$  oz) more for every additional year of the child's age. It should be remarked that unsuccessful results are usually due to the administration of



an insufficient quantity of the drug. So far the largest doses given internally have not caused any dangerous symptoms. In cholera it is recommended to continue giving small doses, 1 teaspoonful of a 40:100 suspension of kaolin every 1 to 2 minutes, without considering the presence of vomiting. Should the vomiting cease and kaolin be seen in the stools, larger quantities amounting to 100 to 150 grammes (3½ to 5 oz) or more should be given at a time. In obstinate vomiting dry kaolin may be swallowed in doses of a quarter of a teaspoonful. In diphtheria a small teaspoonful of a kaolin suspension (40 to 50:100) is given every 2 to 3 minutes until the fever has subsided, and the same dose is continued at least every 10 minutes until the membrane has disappeared. The successful result is apparent within a few hours.

### **Bornyval.**

This recognised sedative has been made the subject of a publication by A. Callivokas who confirms once more its usefulness in nervous excitement of various kinds. The preparation has given very good results in daily doses of 3 to 6 capsules, particularly in neurasthenic anaphrodisia, agoraphobia, anomalies of menstruation, incontinence of urine and hysterical disturbances associated with melancholia, insomnia and excitement. In chronic diseases too it has been found an efficacious auxiliary. In a tuberculous woman suffering from palpitation, this left off immediately on the use of bornyval. In the case of another woman suffering from mitral insufficiency and attacks of giddiness a successful result was obtained within a short time. Appreciable improvement and relief were also apparent after 4 days' treatment in a patient with tuberculous peritonitis coupled with vomiting and attacks of giddiness. By reason of these and similar favourable results the author regards bornyval as a prompt and trustworthy remedy.

### **Bromalin.**

On the elimination of bromine after the internal administration of bromalin no extensive work as yet been done.

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Callivokas, Allgemeine medizinische Zentralzeitung 1910, No. 10, p. 128.

The investigations of E. Bermann and L. Bilinskis are therefore particularly interesting, for they complete our knowledge of the physiology and pharmacology of this valuable bromine preparation. Bermann made her experiments on rabbits which were given bromalin by mouth, usually through a tube. The urine of these animals was tested for bromine by the method advised by Bürgi and Schreiber. It was found that the whole of the bromine taken appeared in the urine in the form of alkaline bromide, while no bromine in organic combination could be detected. From this result it is certain that bromine taken in the form of bromalin is able to exert its full action in the organism, and this accords completely with the favourable results obtained by other authors with the use of bromalin in neurasthenia and epilepsy. Bromalin contains 32 p.c. of bromine. It has already been described several times in these Reports. It is given in doses of 2 to 4 grammes (30—60 grains) several times a day as a sedative and anti-epileptic, and its most important characteristic is the absence of secondary effects following its use.

### **Bromipin.**

The elimination of bromipin, like that of bromalin, has been examined by E. Bermann in animal experiment. Bromipin taken by mouth was found to appear in the urine in one or two days, partly in organic, partly in inorganic combination, though the latter form is greatly in excess. The experiments show that bromipin is gradually split up in the organism, and that the greater part of the bromine contained is able to exert its action. The experiments show further that the preparation does not display its full therapeutic action for some time after its administration, though its action begins to appear earlier, in fact within a relatively very short time. These results agree with the accounts given by various workers of the action of bromipin, and show that it is indicated especially where a prolonged constant and uniform effect is required, rather than an imme-

Bermann-Bilinskis, *Therapeutische Monatshefte* 1910, No. 4, p. 183.  
Bürgi-Schreiber, said by Bermann not to have been published, but given briefly by Bilinskis in *Therapeutischen Monatsheften* 1910, No. 2, p. 76.

\*) Merck's Reports 1897, 1898, 1900, 1906 and 1907.

Bermann, *Therapeutische Monatshefte* 1910, No. 4, p. 185.

diate intense action. Bromipin is mostly used in epilepsy, neurasthenia, whooping-cough and neuralgia. It has already been described in these Reports\*).

Bermann states that the method for the simultaneous estimation of organic and inorganic compounds of bromine suggested by E. Bürgi and Schreiber has not yet been published though it is of particular interest to pharmacologists. We will therefore briefly describe the method given by Bilinskis for the qualitative detection of bromine:

100 c. c. of urine are rendered faintly acid with dilute nitric acid, a slight excess of silver nitrate is added, and it is quickly brought to boiling point and filtered. The precipitate is washed with water containing nitric acid and the washings are added to the filtrate for further examination for organic bromine compounds.

The precipitate is dissolved in ammonia, the solution is filtered and acidified with nitric acid. The precipitate thus obtained is washed and reduced with zinc and sulphuric acid. This solution contains hydrobromic acid, and on the addition of solution of chlorine and shaking with carbon bisulphide the bromine is dissolved by the latter and may be recognised by the colour imparted to the carbon bisulphide.

The filtrate of the silver halogen with the washing water is treated with hydrochloric acid to precipitate the excess of silver nitrate. It is then filtered and the filtrate is nearly neutralised with caustic soda and mixed with an excess of ammonia. After the addition of calcium chloride it is again filtered, a little concentrated soda solution is added to the filtrate, and the mixture is evaporated to dryness. The residue is carefully heated and melted and the fused mass is extracted with water, the extract thus obtained is acidified with hydrochloric acid. The nitrous acid it contains is destroyed by adding solution of urea drop by drop. The solution is then tested for bromine by means of solution of chlorine and carbon bisulphide.

### **Bromural.**

Bromural has been found of very good service as a nervine and hypnotic by Josephsohn in many cases of

\*) Merck's Reports 1897—1908.

Bilinskis, *Therapeutische Monatshefte* 1910, No. 2, p. 76.

Josephsohn, *Allgemeine medizinische Zentralzeitung* 1910, No. 5.



nervous irritability and depression. He prescribed it in headache, giddiness, sleeplessness, buzzing in the ears, palpitation, disturbances of vision, gastric pressure, etc., when these symptoms accompanied hysteria, arterio-sclerosis, chlorosis and myocarditis. In some cases the cause of the symptoms could not be ascertained. In all cases the result was quickly obtained and there were never any troublesome secondary appearances, such as bromide rash.

O. Schäfer obtained such excellent results in neurasthenia, angina pectoris and in cardiac and vascular neuroses that he prescribed bromural in all diseases which were causing insomnia either by reason of the pain accompanying the disease or by setting up a condition of irritation. In fractures and traumatic shock it was also found of good service. In sexual anomalies it produced a general sedative effect, and also tended to prevent gonorrhœal erections.

In sea-sickness, Heinicke observed that the vomiting and the giddiness left off very quickly after the administration of bromural. Even when the sea was rough the patients felt quite well, provided the bromural treatment was assisted by the usual precautionary measures. At first a dose of 0.3 gramme (5 grains) was usually given, and if necessary a second dose of 0.15 gramme ( $2\frac{1}{3}$  grains) half an hour later. The largest dose given by the author was 0.45 gramme (7 grains).

Bromural is useful as a sedative in dental practice. G. J. Dietrich gave it to nervous patients half an hour before treatment to drive away their restlessness and fear. In most cases he was successful. In anæsthesia with ethyl bromide or ethyl chloride, the preparation, when given beforehand, causes the anæsthesia to run a quiet course, and it is said to be a useful remedy after an anæsthetic to prevent nausea and headache. As a hypnotic bromural was found valuable in cases in which patients were unable to sleep after long courses of Plombières baths or as the result of painful wounds. Finally the author recommends bromural for the relief of pain if the application of arsenic has proved insufficient when the pulp is to be exposed.

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Schäfer, Fortschritte der Medizin 1910, No. 23.

Heinicke, Therapeutische Rundschau 1909, No. 44.

Dietrich, Deutsche zahnärztliche Zeitung 1910, No. 4.

**Calcii chloridum.**

Wright's original investigations on the action of calcium chloride on the clotting of blood led to the discovery of valuable new methods of applying calcium salts in therapeutics, e. g., in dealing with the serum disease. Similarly the works of R. Chiari and H. Januschke are sure to enlarge the field of utility of the calcium salts. Januschke has shown that pleural effusions such as may be produced in dogs by iodine poisoning are checked by subcutaneous injections of calcium chloride, showing that the walls of the vessels are to some extent strengthened by the administration of calcium. This result is partly confirmed by the pharmacological investigations of Chiari. He found that by removing calcium the permeability of the walls of the vessels was increased. The authors accordingly tested several other substances which were known to produce pleural effusion with great regularity, viz., diphtheria toxin and thiosinamin. With these substances it was also found that the action was checked by calcium injections. They were also able in animal experiments to prevent completely, or to greatly reduce, the inflammatory oedema of the conjunctiva following the instillation of mustard oil by enriching the organism sufficiently with calcium salts. It is possible that the results of these authors may lead to the use of calcium chloride in transudation and exudation in human medicine. The most efficacious method of application would be by subcutaneous injection.

**Calcii lactas.**

The value of calcium lactate in hæmorrhage from the upper respiratory passages is discussed in a communication by W. K. Simpson. The author made use of the well known property of this calcium salt of increasing the coagulability of the blood. He used it first in a hæmophilic patient for the treatment of severe bleeding from the nose which had refused to yield to other methods of treatment, such as suprarenal substance, calcium chloride, etc. He obtained an excellent

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Wright, *Lancet* 1896, p. 807.

Chiari-Januschke, *Wiener klinische Wochenschrift* 1910, p. 427.

Simpson, *Medical Record* 1909, 25<sup>th</sup> September. — *Deutsche Medizinische Zeitung* 1910, No. 15, p. 256.

result. A striking feature of this case is the fact that the author was not able to obtain a permanent result by means of calcium chloride. It appears certain that the lactate acts better than the chloride under certain conditions which are as yet unknown. Possibly personal disposition may be in part responsible for this. Simpson was particularly well satisfied with calcium lactate treatment in operations, especially in children. Before the removal of adenoids and tonsils he gave 4 grammes (60 grains) of the preparation once or twice a day to adults 3 days before the operation, and continued the treatment for at least 3 days after the operation. He directs that the remedy should be given on an empty stomach, either in the morning or between meals, in water. In children the dose should be reduced to suit their age, and a dose repeated 3 times on alternate days would suffice in most cases. There is no need to be over careful in the use of calcium lactate, particularly if it is given with sufficient water. On the whole the author comes to the same conclusions as to the efficacy of calcium lactate as others before him. Not only does the remedy accelerate the coagulation of blood but as a rule it does so in a specially decided manner in hæmophilia where the coagulation is delayed. The author found the lactate more efficacious than other calcium salts, while it was less irritant and more agreeable to take.

### **Calcii permanganas.**

Based on the experience that calcium permanganate has been of good service in cholera, G. A. Stephens tried it in other forms of gastro-enteritis accompanied by intoxication. He used an aqueous solution, greatly diluted, giving doses of 0.015 gramme ( $\frac{1}{4}$  grain) of calcium permanganate, and he states that he was able to relieve gastro-intestinal disturbances which had refused to yield to treatment with bismuth. The internal use of the remedy was found to be particularly good in chronic and subacute affections of the stomach and intestines, while in acute cases the results were less favourable; when there is fever calcium salts are not tolerated by the patients.

Acting on these results Stephens prescribed calcium per-

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Stephens, *Klinisch-therapeutische Wochenschrift* 1910, No. 6, p. 166.

— *British Medical Journal* 1909, 11<sup>th</sup> Dec., p. 1674.

Stephens, *British Medical Journal* 1910, No. 2576, p. 1166.



manganate in lead poisoning. The dose suggested by him is 0.015 gramme ( $\frac{1}{4}$  grain) repeated 3 times a day. The preparation has a disagreeable taste, and should therefore be given in combination with liquid paraffin in gelatin capsules. Within 2 to 3 weeks this treatment causes the disappearance of the lead line from the borders of the gums, and of the other symptoms of lead poisoning, such as the anæmia, sensitiveness to pressure of the sciatic nerve and weakness of the wrist joint. It is possible that calcium permanganate may also be of use as a prophylactic in persons who have to handle lead preparations, and are therefore exposed to the risk of chronic poisoning.

### Calcii sulphidum.

The use of calcium sulphide in various infective diseases such as scarlet fever, typhoid fever and measles is not new, though I am not able to judge whether it is extensively practised. Recently C. D. Ussher has spoken warmly in its favour since he obtained excellent results from its use. The author assumes that the action of the sulphide is due to the liberation in the blood of sulphuretted hydrogen which then kills the pathogenic bacteria. For this reason he insists that calcium sulphide for therapeutic use should be as pure as possible, and not spoiled by being stored too long. This should go without saying in the case of all drugs. With regard to the hypothesis advanced by the author, this must be left to competent physiologists. Ussher used calcium sulphide in abscesses and tumours in which operation was declined, or where a relapse had occurred after a time. Calcium sulphide was given in doses of 0.015 to 0.03 gramme ( $\frac{1}{4}$ — $\frac{1}{2}$  grain) every 2 hours, and the author reports that the pus and swelling disappeared in the course of 8 days. If the drug causes vomiting the dose must be reduced.

### Camphora.

The value of camphor in peritonitis having already been pointed out by Höhne, H. Hirschel made an extensive trial of it in this complaint. On the day before an extensive

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Ussher, Medical Record 1909, 25<sup>th</sup> September.

Höhne, Münchener medizinische Wochenschrift 1909, No. 49.

Hirschel, Münchener medizinische Wochenschrift 1910, No. 15.

gynæcological operation Höhne injected 30 c. c. of camphorated oil (10 p. c.) to prevent the possible occurrence of post-operative peritonitis. The injection was made below the navel into the abdominal cavity. The author states that in 42 cases he obtained favourable results. He explains the action of this treatment as due to a reactive inflammation of the peritoneum set up by the camphorated oil, causing an accumulation of bactericidal leucocytes. Hirschel used camphorated oil in advanced peritonitis only in cases in which the prognosis was very bad, so that he regards camphorated oil treatment as a last resource. After opening the abdomen and removing the pus, 100 to 300 grammes ( $3\frac{1}{3}$ —10 oz) of a 1 p. c. camphorated oil, previously warmed and sterilised, were introduced and spread over every part of the abdominal cavity, among the coils of intestine and over the sides of Douglas's pouch, using a piece of gauze. In most cases the author made a counter-incision and inserted a suitable drain. No injury to the patients attributable to the camphorated oil was ever observed. The oil treatment has, of course, to be accompanied by suitable after-treatment of the patients. The author lays great stress on the importance of giving an abundant quantity of water in the form of subcutaneous, intravenous and rectal applications of normal saline solution. Proper evacuation of the bowels must also be obtained either by enemata or by injections of physostigmine, while vomiting must be treated by washing out the stomach. Hirschel's results encourage further trial.

A case of the formation of keloid after injections of camphorated oil is reported by E. Braendle. The keloids appeared about two years after the camphor treatment, and must be regarded as a consequence of the puncture made in giving the injection. Details of this case will be found in the original paper.

### Carbenzyme.

E. Falk and A. Sticker have found that vegetable carbon is particularly adapted for absorbing ferments, the action of which may be readily transferred from the carbon

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Braendle, *Dermatologische Zeitschrift* Vol. 16, No. 12. — *Deutsche Medicalzeitung* 1910, p. 356.

Falk-Sticker, *Münchener medizinische Wochenschrift* 1910, No. 1, p. 4. — *Berliner klinische Wochenschrift* 1910, No. 23, p. 1049.

to various albuminous solutions. They therefore used a vegetable carbon which had absorbed sterile trypsin for therapeutic purposes. This preparation, known as carbenzyme, was first tested by them on animals with the result that it was found that intravenous injections had a favourable effect on tumours. Its introduction into therapeutics was therefore justifiable. Trypsin, in combination with carbon, might be expected to produce a slow, long-continued action as the trypsin was gradually set free from its combination with carbon by the presence of albuminous substances. The internal use of carbenzyme was limited to experiments after laparotomy. The troubles which frequently occur in the first days following laparotomy as the result of the accumulation of gases were materially diminished by giving one tablet every 3 hours. In meteorism, again, when due to post-operative adhesions, a favourable result was obtained. For the cure of fistulous passages the authors used a fine emulsion prepared by rubbing up carbenzyme powder with a 0.5 p. c. soda solution. This was injected by means of a syringe. In inoperable malignant tumours carbenzyme injections frequently produce extensive disintegration and absorption of large tumours in a short time. However, the cure of an inoperable carcinoma is no more to be expected than by trypsin treatment, for carbenzyme appears to act differently upon malignant tumours and seems to have a far more powerful action upon sarcomata than upon the tumours of epithelial origin. For the purpose of repeating these tests the authors recommend for internal use the administration of 3 to 5 carbenzyme tablets daily, and for subcutaneous use an emulsion of 0.5 gramme ( $7\frac{1}{2}$  grains) of carbenzyme with 10 c. c. ( $\frac{1}{3}$  oz) of 0.5 p. c. sterile soda solution. The preparation may also be applied externally as a dusting powder to be spread upon wounds which refuse to heal. The pain produced by the injection of carbenzyme may be diminished by a preliminary injection of cocaine.

Good results are obtained by local injections of carbenzyme in tuberculous affections such as tuberculosis of bone, of joints, of mucous sacs, etc. Zur Verth found them to have a favourable action in surgical tuberculosis.



The reaction following an injection, apparent in the foci treated, resembles that following iodoform-glycerin injections, while the curative effect appears to be even greater. A single injection of a thin suspension was made and was repeated if necessary after several weeks. In tuberculosis of the soft parts it is advisable to inject small quantities only of carbenzyme, for large doses of powdered carbon may occasionally give rise to bed sores.

H. Rotky tested the action of carbenzyme in a number of cases of gastro-intestinal catarrh, and found the preparation a very useful remedy in hyperacidity and severe diarrhoea of tuberculous origin. In these affections he obtained an improvement; it is true this was in part transitory and consisted in a relief of the subjective symptoms. The drug had no effect on the flatulence, gastric hæmorrhage and constipation. The author does not therefore consider carbenzyme, when given internally, to possess the importance attributed to it by Falk and Sticker, though he believes that it will prove of good service when applied externally to ulcers.

### **Carbo animalis.**

Last year I reported on the use of animal carbon in poisoning by fungi, and by vegetable and mineral poisons\*). O. Muck pointed out recently that carbon gives good results in suppuration. This observation is not new\*\*), but the author thinks it should be used more frequently in the treatment of granulating wounds of bone in otological surgery, especially in dealing with that enemy to the growth of epidermis and excitor of perichondritis auriculæ: the bacillus pyocyaneus. Hohn has proved experimentally that animal carbon absorbs the volatile substances of this bacillus, and greatly impairs the growth of the bacillus in its dry state, though in the moist state no inhibitory effect is produced. Muck therefore used dry powdered animal carbon in the after-treatment of radical operations on the mastoid process with the idea of protecting the young growing epidermis, and guar-

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Rotky, *Therapeutische Monatshefte* 1910, No. 10, p. 530.

\*) Merck's Reports 1909, p. 157.

Muck, *Münchener medizinische Wochenschrift* 1910, No. 6, p. 297.

\*\*) See *Deutsche medizinische Wochenschrift* 1883, p. 685.

Hohn, quoted by Muck l. c.

ding against maceration by preventing discharge. He reports the following case: A very large cavity in the mastoid bone left after a radical operation had been dealt with by a secondary plastic operation (Körner's method) and the flap had healed. After 8 days he filled the cavity with powdered animal carbon. The dressing was then left for 5 days without a plug. On removing it a mass of carbon of the consistency of soft wax was found to adhere to the dressings, while there was scarcely any pus in the cavity. A complete covering of epidermis was obtained within 6 weeks. In another case the author observed the use of animal carbon to be followed by a very rapid growth of epidermis. He also noticed that the fœtor disappeared very quickly. As soon as the formation of epidermis was completed he left the dressing with animal carbon for 8 days at a time without change of dressings.

#### **Chinolini sulphosalicylas.**

The chinoline salt of sulphosalicylic acid is described by G. Prunier as a white compound, crystallising in needles of a silky lustre, of the composition  $C_6H_3 \cdot SO_3H \cdot OH \cdot COOH \cdot C_6H_7N + N_2O$ . The preparation is readily soluble in hot water and in alcohol. In cold water it dissolves only in the proportion of 3:200. It is almost insoluble in ether, chloroform, benzol and acetone. At about  $110^{\circ}C$ . it loses its water of crystallisation, and it melts at  $220^{\circ}C$ .

Prunier regards this new preparation as a powerful disinfectant which has been shown by pharmacological experiments on animals to be less poisonous than quinine sulphosalicylate. The lethal dose was estimated by him to be 0.29 to 0.34 gramme per kilogramme of animal, both on subcutaneous and intravenous application. Its antiseptic and bactericidal power is approximately equal to that of carbolic acid. The author has given no indication as to the manner in which chinoline sulphosalicylate is to be used therapeutically.

#### **Chloral hydrate.**

Of the various substances recommended for commencing chloroform anæsthesia, chloral hydrate deserves our fullest

Prunier, *Journal de pharmacie et de chimie* 1910, I, p. 538. —  
Union pharmaceutique 1910, p. 254. — *Nouveaux remèdes* 1910,  
p. 351.

attention. P. Delbet and R. Dupont report on 850 cases of chloroform anæsthesia in which chloral hydrate was used. They found it to possess advantages even over scopolamine. In doses of 4 grammes (60 grains) it is non-poisonous, while it prevents the stage of excitation before the anæsthesia, or at any rate greatly reduces it. The patient passes into a somnolent state after taking this dose, and almost invariably enters the operating room in this condition, when he is readily and quickly anæsthetised by chloroform. In men anæsthesia is usually complete within 10 minutes, in women within 8 minutes, while after 0.001 gramme ( $\frac{1}{64}$  grain) of scopolamine, anæsthesia is obtained several minutes later. Vomiting is equally frequent after the anæsthesia whether chloral hydrate or scopolamine are used.

With regard to the analysis of chloral hydrate for impurities, it is easy to make the test more stringent, as is already done in the case of chloroform. The German pharmacopœia has done rightly in substituting for the sulphuric acid test for chloroform one with formaldehyde and sulphuric acid. Admittedly it is not yet certain which impurities are detected by the formaldehyde-sulphuric acid test, but the impurities being unknown it is impossible for us to say whether they are noxious or indifferent substances. It is therefore very desirable to ensure their absence in chloroform, and the same applies to chloral hydrate. In this case the pharmacopœia has retained the old test with sulphuric acid. As it is necessary to ensure the greatest degree of purity in all medicinal remedies, as far as this is technically possible without raising the price out of all proportion, the more accurate test with formaldehyde-sulphuric acid should be regarded as the normal one in the case of chloral hydrate. The chloral hydrate issued by me therefore complies with the following test: If 2 grammes of chloral hydrate are dissolved in 10 c.c. of sulphuric acid (Sp. gr. 1.84) and 4 drops of formaldehyde (40 p. c.) are added, no colour should appear within half an hour; a glass-stoppered bottle is used previously rinsed out with sulphuric acid.

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Delbet-Dupont, *Revue de chirurgie* 1910, 10<sup>th</sup> June. — *Klinisch-therapeutische Wochenschrift* 1910, p. 682.

\*) See Stadlmayr, *Zeitschrift für angewandte Chemie* 1910, p. 1546.



Particulars of the average dosage of chloral hydrate in veterinary practice have been given by Mendel, who describes a case in which a thoroughbred horse was to be anæsthetised with chloral hydrate for the application of the cautery. 150 grammes (5 oz) of the preparation had practically no effect; accordingly next day 180 grammes (6 oz) were given and in addition 0.4 gramme (6 grains) of morphine hydrochloride was injected. In spite of this the animal showed sensitiveness to pain and resisted vigorously during the burning. As the horse suffered no injury from the treatment the author believes that the maximum dose of chloral hydrate given by Kröning, Scheidling, Nitzschke, Dreger, Kämper and others (25 to 100 grammes [ $5\frac{5}{6}$ — $3\frac{1}{3}$  oz]) would under some conditions produce no more than a short anæsthesia in horses, so that when the remedy displays only a slight action the maximum dose may be exceeded without danger.

### **Chloro-Meta-Cresol.**

A short communication by Laubenheimer shows that a 0.5 p.c. solution of chloro-meta-cresol in 70 p.c. alcohol has proved an excellent agent for disinfecting the hands. The investigations of the author show chloro-meta-cresol to be an extraordinarily powerful bactericide, while it has a relatively slight toxic effect. By using the alcoholic solution it was possible to render the hands completely free from germs in a large percentage of his trials. The preparation accordingly fulfils all the requirements of surgeons as an agent for disinfecting the hands. It takes less time than the more popular method of Fürbringer. Its action is certain, and in the above solution it has no smell, and no irritant action.

It is difficult to judge whether the preparation used by Laubenheimer in his experiments was a pure mono-chloro-meta-cresol or a technical product, and which of the four theoretically possible chlorine substitution products of meta-cresol it was. As far as I know the only preparation on the market is para-chloro-meta-cresol.

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Mendel, Zeitschrift für Veterinärkunde 1910, No. 7, p. 334.

Laubenheimer, Deutsche medizinische Wochenschrift 1910, No. 4, p. 199.

E. Konrad used chloro-meta-cresol and obtained very good results with it. The preparation used by him was a soap solution containing chloro-meta-cresol (known as lyso-chlor). He regards chloro-meta-cresol as an excellent disinfectant, especially adapted as an improvement on von Herff's rapid method of disinfection. It has a powerful bactericidal action, and only slightly toxic properties. The author therefore feels justified in recommending it as an antiseptic for irrigations.

T. Ikada also expresses a very favourable opinion as to the value of chloro-meta-cresol. He regards the preparation as superior to all other known agents for disinfecting the hands.

### **Chloroform.**

The article on "ether"\*) in these Reports shows that the intravenous application of ether, as recommended by Burkhardt, has found little application as yet. A similar method of using chloroform is described in one communication only, by Giani. This author reports two operations which ran a good course under intravenous infusion of chloroform. The author used a mixture containing 0.6 gramme of chloroform in 100 c. c. of normal saline solution. Of this he injected about 50 c. c. in the first minute, and 1100 to 1500 c. c. in all. At the end of 3 minutes unconsciousness intervened, and after 5 minutes complete relaxation with abolition of the corneal reflex; the total duration of the anæsthesia was 40 minutes, during which time the respiration was quiet and the pulse quite regular. The total amount of chloroform used amounted to 6.6 to 9 grammes. Vomiting did not occur, and on the afternoon of the day of the operation there were only traces of albumin in the urine, and these disappeared by the night. The urine contained no casts, white blood corpuscles or elements from the kidneys. The author made no observations to determine whether thrombi were formed at the seat of the puncture. He states that he occasionally slowed the rate of flow of the

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Konrad, Archiv für Gynäkologie Vol. 91, No. 2.

Ikada, Dissertation. Gießen 1910.

\*) See p. 78.

Giani, Policlinico 1909, No. 51. — Münchener medizinische Wochenschrift 1910, p. 870.

infusion, and from time to time interrupted its flow. The number of his cases is far too small to allow us to decide whether chloroform is better suited for intravenous injection than ether. The author intends to publish further results.

J. Eisenberg was able, in small operations and in confinements, to produce by means of small quantities of chloroform (10 to 15 drops) a condition in which the sensibility to touch and heat were considerably reduced, while in some cases there was complete abolition of sensibility to pain. This "chloroform half-sleep" is recommended by him to the notice of surgeons. The view of Hallauer and others that the condition depends on suggestion is denied by Eisenberg.

Of interest are the communications of E. Levi, according to which the inhalation of a mixture of carbonic acid and oxygen may, under some circumstances, be of great value in chloroform anæsthesia. The author made use of the known physiological fact that the respiratory centre reacts very readily to the slightest alterations in the carbonic acid pressure of the blood; he made experiments to ascertain how the automatic functions of the bulbar respiratory centres would behave under the toxic influences produced by a mixture of carbonic acid and oxygen. It was found that even in cases of severe depression or absolute abolition of the function of the respiratory centre, respiration was immediately started again by this mixture. G. Crescenzi and O. Marchetti, who sought to apply these results practically by giving inhalations of carbonic acid mixture in chloroform anæsthesia, obtained very satisfactory results. As soon as respiration began to become slower during chloroform anæsthesia or to become somewhat superficial, or when respiration threatened to stop, without interrupting the anæsthesia, Crescenzi allowed a stream of mixed carbonic acid and oxygen (30+70) to pass under the mask for a few seconds. The action appeared at once, respiration becoming more regular and

Eisenberg, *Zentralblatt für Gynäkologie* 1910, p. 659.

Levi, *Rivista critica di clinica medica* 1910, p. 465. — *Klinisch-therapeutische Wochenschrift* 1910, No. 40, p. 957.

Crescenzi, *Klinisch-therapeutische Wochenschrift* 1910, No. 40, p. 960.

Marchetti, *Klinisch-therapeutische Wochenschrift* 1910, No. 40, p. 961.



more frequent. The method is of special advantage if it be desired to keep a patient for some time in a state of light anæsthesia. If deeper anæsthesia is required it is merely necessary, while continuing the inhalation of chloroform, to give a few breaths of the mixture to bring about a state of deep respiration in a few seconds, which enables a larger quantity of chloroform to be inhaled. Thus the desired effect is achieved with less chloroform and in a shorter time than is the case under ordinary conditions. Marchetti also states that this method is of great value, and is a perfectly harmless auxiliary to chloroform anæsthesia, as it makes it possible to prevent the apnœic conditions which frequently occur during chloroform anæsthesia, or to effectually treat such conditions.

### **Cholesterin.**

Since it has been found that cholesterin plays the part of a protective body against hæmolytic substances in the organism, rendering the toxins harmless, neutralising hæmotoxins and neurotoxins, and taking an important part in tetanus, its therapeutic use has grown in importance\*). Especially in the treatment of anæmia the value of the preparation has been recognised. J. Chevalier found its action well marked in cases in which iron and arsenic treatment failed, cholesterin producing a rapid improvement in the general condition. In enteritis due to intestinal infection the author also obtained good results from the use of this remedy. In his experience the results are better when it is given by mouth than when administered subcutaneously. The dose for adults amounts to 1 or 2 grammes (15—30 grains) a day. It may be considered as good as certain that the parasites of malaria produce hæmolytic toxins. Hence Grimm's suggestion to use cholesterin therapeutically in black-water fever appears fully justified. Some experiments by the author led to the conclusion that the administration of 3 grammes (45 grains) a day gives good results. A definite opinion as to the value of cholesterin in black-water fever cannot be expressed until further trials

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\*) Merck's Reports 1901, 1905, 1907, 1908 and 1909.

Chevalier, Bulletin général de thérapeutique 1910, No. 1.

Grimm, Deutsche medizinische Wochenschrift 1910, No. 4.

have been made. L. Külz and Seiffert made some trials which confirm Grimm's results.

Cholesterin is also worth trying in neurasthenia and tuberculosis. Very satisfactory results are reported by R. Novoa. He treated his patients systematically with this remedy, given by mouth or subcutaneously, in an aqueous emulsion or in an oily solution. As a rule he began with daily doses of 0.5 gramme ( $7\frac{1}{2}$  grains) and increased the amount intermittently to 5 grammes (75 grains). This treatment gave good results in anæmia.

### Choline.

Important contributions to the physiological action of choline have been made by E. Abderhalden, F. Müller, F. Schenk, L. B. Mendel and F. P. Underhill. Abderhalden, as well as Mendel and Underhill, oppose the statements of Modrakowski that choline raises the blood pressure. The view expressed some time ago by Lohmann is thus confirmed by them. Abderhalden's investigations show that the occasional occurrence of a rise of blood pressure after choline injections is not due, as Modrakowski says, to a chemical impurity or decomposition of the choline. He obtained a fall of blood pressure in 39 cases, a rise in only 3 cases. In these the author explains the rise by the animals' restlessness due to incomplete anæsthesia, or, if the anæsthesia be deep, he attributes it to the muscular contractions caused by the choline. For choline produces general excitation, overcoming anæsthesia and curare paralysis. As soon as the contractions left off the blood pressure fell. For this reason the author regards a fall of blood pressure as

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Külz, *Archiv für Schiffs- und Tropenhygiene* 1910, Vol. 14, p. 739.  
Seiffert, quoted by Grimm, *Archiv für Schiffs- und Tropenhygiene* 1910, Vol. 14, p. 743.

Novoa, *Gaceta médica del Sur d'España* 1910, No. 3.

Abderhalden, *Medizinische Klinik* 1910, No. 22, p. 883.

Müller, *Pflügers Archiv für die gesamte Physiologie* 1910, (Vol. 134), p. 289.

Schenk, *Deutsche medizinische Wochenschrift* 1910, No. 24, p. 1130.

Mendel-Underhill, *Zentralblatt für Physiologie* 1910, (Vol. 24) p. 251.

Modrakowski, *Pflügers Archiv für die gesamte Physiologie* 1908, Vol. 124, p. 601.

Lohmann, *Zentralblatt für Physiologie* 1909, Vol. 23, p. 291.

the typical action of choline. Müller attempted to explain experimentally the fact that atropine reverses the typical action of choline so that when injected previously the action of choline is transformed into one producing a rise of blood pressure. His experiments show that the fall of blood pressure is undoubtedly due to the combination of congestion in the heart with peripheral vaso-dilatation. The reversal of the choline action by atropine is due, in the author's opinion, to the fact that choline is entirely prevented from manifesting its action after atropine, or that it causes vaso-constriction. This result and others point to the fact that choline by itself influences the autonomous vaso-dilator and vaso-constrictor elements in the walls of the vessels in such a way that the vaso-dilator stimulus is almost always in excess, atropine paralysing the vaso-dilator elements so that only the constrictor elements are manifested.

Schenk has tested the action of choline on pregnancy in animal experiments. It is well known that von Hippel and Pagenstecher, as well as Werner and Lichtenberg, found that injections of choline had an injurious effect on pregnancy in rabbits. Schenk's experiments led him to doubt whether choline possesses a specific action in this direction, the injurious influence on the pregnancy being far more probably due to the trauma produced by repeated injections. He found he could cause interference with the course of pregnancy almost as frequently by an injection of an indifferent substance (sodium sulphate) as by injections of choline.

### **Chrysarobin.**

A closer insight into the oxidation processes which chrysarobin undergoes on the skin is afforded by the interesting experimental results published by P. G. Unna and L. Golodetz. They found that chrysarobin when oxidised yields not only chrysophanic acid but two other substances, oxy-chrysarobin and chrysaloxin. These three oxidation products are distinguished by their spectra. Chrysarobin in benzol

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Hippel-Pagenstecher, Merck's Reports 1907, p. 74.

Werner-Lichtenberg, Deutsche medizinische Wochenschrift 1906, No. 39, p. 1583.

Unna-Golodetz, Monatshefte für praktische Dermatologie 1910, Vol. 51, p. 1. — British Medical Journal 1910, No. 2603, p. 1593.



solution shows a spectrum characterised by two separate lines in the green, oxychrysarobin shows a diffuse line in the green and one in the yellow, chrysalexin a dark line in the red. Oxychrysarobin is formed by the alkali-free oxidation of chrysarobin by means of linseed oil, oleic acid, oleate of lead or benzoyl peroxide, and also spontaneously in alkali-free chrysarobin ointments applied to the skin. Chrysophanic acid is formed by a brief oxidation of chrysarobin in the presence of basic substances, chrysalexin by a more prolonged oxidation under similar conditions. Alkali-free chrysarobin preparations (ointments, varnishes, etc.) form on the skin oxychrysarobin, a change due to the normal presence of oleic acid on the skin. The presence of oleic acid on the palms of the hands, and on the soles of the feet is due to minute drops of oleic acid from the sweat glands, its oxidising action may be demonstrated by the blue colour produced in rongalite white. In other parts of the body the oleic acid is excreted by the sebaceous and aggregated glands.

Directions for the treatment of psoriasis by chrysarobin are given by Graham Little. For ambulatory treatment he recommends an ointment consisting of 1 to 2 grammes (15—30 grains) of chrysarobin, 7.5 grammes ( $\frac{1}{4}$  oz) of kaolin, 15 grammes ( $\frac{1}{2}$  oz) of starch, 15 grammes ( $\frac{1}{2}$  oz) of lanoline and 7.5 grammes ( $\frac{1}{4}$  oz) of liquid paraffin. This is applied at night and removed in the morning by means of vaseline or benzine. Small efflorescences on the face are treated with the following ointment: 3 grammes (45 grains) of chrysarobin are worked into sticks with 5 grammes (75 grains) of lanoline and 2 grammes (30 grains) of white wax. In acute and obstinate cases of psoriasis the patient must remain in bed for 4 weeks. The whole body except the face is treated with chrysarobin ointment until the skin begins to peel. At the same time arsenic treatment is used internally.

M. Oppenheim has used the chrysarobin salicylic soap ointment recommended by Dreuw in psoriasis vulgaris with success, and he therefore regards it as a material improvement in the use of chrysarobin in this disease. Its use appears specially indicated in cases of chronic psoriasis vulgaris of

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Little, *Lancet* 1910, No. 4517, p. 852.

Oppenheim, *Österreichische Ärzte-Zeitung* 1910, No. 12, p. 261.

Dreuw, *Merck's Reports* 1909, p. 165.

a local kind, and in chronic psoriasis nummularis when the skin has become somewhat resistant by unsuccessful treatment with other remedies. This treatment is contra-indicated in acute psoriasis, when the skin is sensitive, and when there is an idiosyncrasy to chrysarobin.

### **Cocainæ hydrochloridum.**

A conclusion of some practical importance was arrived at by A. Fröhlich and O. Loewi after their experiments with cocaine and adrenalin. They found that the action of adrenalin in raising the blood pressure after subcutaneous injection is displayed with great certainty, and with enormously increased intensity and duration, on the simultaneous application of minimal doses of cocaine—doses too small to produce any action by themselves. This fact was ascertained by the authors as regards the action on the blood vessels, the urinary bladder and the eye. Another combination of cocaine with adrenalin and corticin\*) is recommended by J. Ascher for the treatment of hay fever and hay fever conjunctivitis. A solution of corticin (1:100) was used years ago by Boesser as a lotion for the affected mucous membranes. Ascher, assuming that the eyes are the actual port of entry of the hay fever infection, about 3 weeks before the beginning of the hay fever season, instils eye drops of the following composition:

Rp. Cocain. hydrochlor.	0.15 gramme	(2 $\frac{1}{3}$ grains)
Adrenalin (1:1000)	0.15 „	(2 $\frac{1}{2}$ min.)
Corticin.	0.30 „	(5 grains)
Aq. destill.	30.0 grammes	(1 oz).

Of this 4 to 6 drops are instilled into both eyes, at first 3 times a day, later 4 to 6 times; the drops must enter the lachrymal canals to enable them to exert their action on the nasal mucous membrane as well. In addition, the nasal mucous membrane is painted with 10 to 20 drops of the above solution diluted with a cupful of lukewarm water.

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Fröhlich-Loewi, Archiv für experimentelle Pathologie und Pharmakologie 1910, Vol. 62, p. 159.

\*) Corticin is a mixture of 1 part Caffeine and 2 parts Quinine hydrochloride, see Merck's Reports 1906, p. 68.

Ascher, Wochenschrift für Therapie und Hygiene des Auges 1910, No. 47, p. 385.

Boesser, Merck's Reports 1906, p. 68.

Shortly before the critical period the drops are increased in strength by taking about double the quantity of the substances in 30 grammes (1 oz) of water. This treatment is said to have an excellent action. With the exception of a single case in which the treatment was probably not carried out according to the directions, the author observed either the complete absence of the hay fever or of the hay fever conjunctivitis, or, if the attacks came on, they soon passed off as the result of continued energetic treatment. When hay fever is actually present the remedy is still of good service.

In rhino-laryngological practice M. Senator has returned to cocaine, having convinced himself that alypin and novocaine have not proved so successful as anæsthetics, so that he has come to the same result as F. Bruck. These newer remedies fail especially if reflex sensibility is to be abolished for operations on the throat, and for this purpose cocaine is well known to be excellent. Even in combination with adrenalin, alypin and novocaine cannot replace cocaine.

Communications made by Caussade, Chauffard and Soucques on December 24<sup>th</sup>, 1909, to the Société médicale des Hôpitaux show that epidural injections of cocaine hydrochloride form an excellent remedy for the treatment and cure of sciatica. Caussade in acute paroxysmal sciatica used doses of 0.01 to 0.02 gramme ( $\frac{1}{6}$ — $\frac{1}{3}$  grain) and obtained a complete success after a single application. In chronic cases the injection needs to be repeated at intervals of 3 to 8 days. If necessary the doses may be increased to 0.06 to 0.08 gramme ( $1$ — $1\frac{1}{3}$  grains) for the relief of severe pain. Chauffard states that 2 to 3 injections of 0.02 to 0.03 gramme ( $\frac{1}{3}$ — $\frac{1}{2}$  grain) are usually sufficient to effect a complete cure.

To prevent cardiac disturbance due to irritation of the pericardium, M. Heitler recommends cocainizing the per-

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Senator, Münchener medizinische Wochenschrift 1910, No. 10, p. 524.

Bruck, Merck's Reports 1909, p. 169.

Caussade, Chauffard, Soucques, Klinisch-therapeutische Wochenschrift 1910, No. 5, p. 141. — Journal de médecine de Paris 1910, 16<sup>th</sup> July.

Heitler, Medizinische Klinik 1910, No. 25, p. 974.



icardium by means of a 10 p. c. cocaine solution in operations on the heart. For particulars the original paper must be consulted.

### Coryfin.

Papers on this preparation have been published by Braitmaier, Säg and Selbiger. Braitmaier found it an excellent remedy for neuralgic and rheumatic headache. It is specially useful in the dull headache occurring in nervous debility, or irritability rendering mental work impossible. The author warns against the too vigorous application of the remedy. In cold in the nose he directs that a drop of coryfin be placed on wool and introduced into the front of the nasal cavity, in cough, inhalations of the preparation dropped upon hot water give rapid relief. In the latter case the application also gives good results in the form of bonbons. Selbiger also tried coryfin in a large number of cases, and his results are entirely favourable to the use of the remedy. He found it very useful in hypertrophic rhinitis and catarrh of the frontal sinuses. After applying it to the nasal mucous membrane there was always a marked diminution of the swelling. Injected into the larynx, coryfin, even undiluted, causes no appreciable inflammation, while its cooling and anæsthetic action was always found agreeable by the patients. The author considers a 20 to 30 p. c. dilution more suitable. In general for injection into the larynx he uses a mixture of 10 grammes ( $\frac{1}{3}$  oz) of coryfin with 10 grammes ( $\frac{1}{3}$  oz) of liquid paraffin and 1 gramme (17 min.) of oil of eucalyptus.

Säg reports his experiences with coryfin in otological practice. He found it of good service in pruritus of the external auditory meatus, provided the itching is not due to diabetes. For this purpose a swab of wool of the size of the auditory meatus is dipped into pure coryfin solution and then placed in the well cleansed meatus. If necessary this application may be repeated 2 or 3 times a day. The remedy fails if the itching is due to eczema. It was also found very useful in furunculosis of the external

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Braitmaier, *Therapie der Gegenwart* 1910, No. 3.

Säg, *Budapesti Orvosi Ujsag* 1910, No. 7.

Selbiger, *Deutsche medizinische Wochenschrift* 1910, No. 18.

auditory meatus both in the diffuse and in the circumscribed form, and in the intense pain of folliculitis in the external auditory meatus. A combination of coryfin and spirosal may be used with advantage in the treatment of furunculosis. Sæg as a rule prescribed a mixture of equal parts of both drugs.

Caspars confirms the usefulness of coryfin when applied in the form of ointments and gargles in hypertrophic and atrophic catarrh, hay fever and acute coryza, and also in pharyngitis and in itching in the auditory meatus.

A solution of 1 gramme (15 grains) of anæsthesin in 20 grammes ( $\frac{2}{3}$  oz) of coryfin was used by E. Baumgarten with excellent results in tuberculous perichondritis; the entire pharyngeal roof and the infiltrated oedematous ary-epiglottic folds were painted with this solution. The difficulty in swallowing subsided at once and the patients were able to take food. Less unpleasant and of equally good effect are applications to the affected parts of 20 to 25 drops of the anæsthesin-coryfin solution. A similar effect is obtained with the use of a solution of 1 gramme (15 grains) of cycloform in 25 grammes ( $\frac{5}{6}$  oz) of coryfin.

### **Cuorin.**

A few years ago Erlandsen obtained a substance from the heart muscle of oxen to which he gave the name of cuorin, and he described his method in detail. It is a preparation chemically allied to lecithin, a di-phosphatide of the composition  $C_{17}H_{125}NP_2O_2$ . It readily undergoes alteration through auto-oxidation, and is very hygroscopic. Unaltered, active cuorin is soluble in ether, but sparingly soluble in water. Oxidised cuorin is insoluble in ether, but readily soluble in water.

V. Teruuchi and H. Toyoda found in cuorin a preparation which may be used as a test for syphilis. For this purpose they dissolve the preparation in water in the proportion of 0.3:100. To carry out the serum reaction,

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Caspars, *Journal médical de Bruxelles* 1910, No. 27.

Baumgarten, *Medizinische Klinik* 1910, No. 44.

Erlandsen, *Zeitschrift für physiologische Chemie* 1907, Vol. 51, p. 71.

Teruuchi-Toyoda, *Wiener klinische Wochenschrift* 1910, No. 25, p. 919.

the serum to be tested is diluted with 5, 10, 20 and 40 times its volume of normal saline solution, and 0.5 c.c. of each dilution is added to 0.5 c.c. of the reagent, and left at 37° C. for 2 hours (or with serum of feeble action for several hours). The serum of most laboratory and domestic animals, with the exception of that of monkeys and rabbits, gives a precipitate with this reaction. A positive reaction is also obtained in human syphilis, in malaria and leprosy, a negative reaction in syphilis in the first stage, in tuberculosis, typhoid fever, beri-beri, gonorrhœa and in healthy persons. These results led the authors to believe the cuorin serum reaction to be worthy of further investigation for the diagnosis of syphilis. In comparing the reaction with the syphilis reaction of Wassermann they obtained corresponding results in most cases.

### Cupferron.

Baudisch recommended cupferron (nitroso-phenyl-hydroxylamine-ammonium) for the quantitative analysis of iron and copper salts. Its use was briefly described in last year's Reports\*), and has since been further tested by H. Biltz and O. Hödtke, and also J. Hanus and A. Soukup\*\*).

Biltz and Hödtke found that the precipitation of iron may be produced even in a strongly acid solution, and even in the presence of 20 c. c. of concentrated hydrochloric acid to 100 c. c. of the iron solution. Their experiments show that cupferron is a reliable reagent for precipitating not only iron in solution by itself, but also iron in solution in the presence of nickel and chromium salts. The separation of copper from zinc and cadmium salts was very successfully carried out by the use of cupferron. The authors therefore conclude that the new method of precipitation is admirably suited for numerous analytical purposes. Its chief value de-

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Baudisch, *Chemiker-Zeitung* 1909, p. 1298.

\*) See Merck's Reports 1909, p. 174.

Biltz-Hödtke, *Zeitschrift für anorganische Chemie* 1910, Vol. 66, pp. 426.

Hanus-Soukup, *Zeitschrift für anorganische Chemie* 1910, Vol. 68, p. 52.

\*\*) Cupferron has explosive properties; I am therefore no longer able to issue it.



depends on the facility with which iron may be separated from aluminium, chromium and sulphuric acid. On the other hand the separation of iron and copper from silver, mercury, lead and tin appears to be excluded, for these metals are also precipitated by the reagent.

R. Fresenius found the cupferron method suitable for the estimation of iron in the presence of aluminium, chromium, manganese, nickel, cobalt, zinc and alkaline earths. It is therefore a good method for determining iron in weighed precipitates of iron and aluminium oxide, or in precipitates of iron and aluminium phosphate. The method is undoubtedly more convenient and more certain than separation by caustic potash, while it has decided advantages over the method of separation by means of tartaric acid and ammonium sulphide.

Hanus and Soukup found that copper may be estimated in acid solutions, and in the presence of a large excess of the reagent by means of cupferron. It is necessary to filter the copper precipitate immediately, for on standing part of the copper may redissolve. In the filtrate, cadmium or zinc may be precipitated after oxidising the excess of cupferron by means of nitric acid, for sodium carbonate brings them down as a basic salt. The single determinations described by the authors differ in some respects from those of Baudisch; the original papers must be consulted for further details.

### Cycloform.

Cycloform is the isobutyl ester of para-amido-benzoic acid, a white crystalline powder, melting at 65° C., sparingly soluble in water, readily soluble in alcohol and ether. E. Impens has shown that this new local anæsthetic has the advantage that it dissolves in water only to the amount of 0.022 p. c. This sparing solubility leads to an entirely local action and prevents symptoms due to absorption. Its anæsthetic power is said by the author to be very great, for he found that a saturated aqueous solution, when dropped upon the cornea of a rabbit's eye, produced complete loss of sensitiveness within 2 minutes, and lasting about 10 minutes.

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Fresenius, *Zeitschrift für analytische Chemie* 1911, Vol. 50, p. 35.

(See also H. Weber, *ibid.* p. 50.)

Impens, *Thérapie der Gegenwart* 1910, No. 8.

A saturated solution diluted with double its volume of water is said still to possess definite anæsthetic power. Moreover it has no caustic properties and does no harm to the protoplasm.

A. Most tested the preparation in superficial wounds and ulcers, for instance in burns, painful granulations, and painful ulcers of the leg. He never saw any harmful effects produced by the remedy, it displayed no irritant or caustic action, and the pain was never increased by its application. Its action never failed except occasionally when applied in the form of an ointment. Two patients complained of increased pain after the use of cycloform ointment, but these were uncontrollable cases of paronychia and ulcer of the leg where the patients had applied the dressings themselves, and in both cases the drug had been of good service previously. In many cases the ointment displayed an excellent action. After using cycloform ointment in vain the author occasionally obtained good results by changing to dry treatment with cycloform. For this reason he attributed the want of success, not to the preparation, but to the unsuitable method of using it. Treatment with powdered cycloform gave complete satisfaction to most of his patients, particularly in cases of painful ulcer of the leg. M. Strauss also obtained an excellent sedative action with the use of a 5 to 10 p. c. cycloform ointment in pain due to wounds, burns, ulcers of the leg and superficial carcinoma. He found it a perfectly harmless, non-irritant anæsthetic for wounds, while it did not delay healing. M. O. Wyss found the anæsthetic action of cycloform unsatisfactory in painful wounds, whether used in the form of a powder or of an ointment. On mucous membranes the action was also found insufficient, though in inoperable carcinoma of the rectum, in hæmorrhoids, anal fissures and pruritus ani very satisfactory results were obtained from its application in the form of a 20 p. c. ointment, and in the form of suppositories (containing 0.3 gramme [5 grains] each.) Impens has shown that cycloform has the power of preventing decomposition, and that it has a slight ger-

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Most, Heilkunde 1910.

Strauss, Münchener medizinische Wochenschrift 1910, No. 50.

Wyss, Archiv für Verdauungskrankheiten, Vol. 16, No. 5.

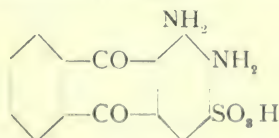
micidal action. This is now confirmed in the treatment of wounds, for Most found that malodorous and unclean wounds improved in appearance within a few days under treatment with cycloform powder and sterile dressings. The wounds became clean, the discharge diminished and new granulations formed. A. Zeller obtained satisfactory results with the use of cycloform in burns, painful rhagades on the hands, in chronic eczema, anal fissures, intertrigo and commencing bedsores, also after operations for hæmorrhoids and in ulcers of the leg. In eczema connected with fæcal fistulæ the preparation proved of good service. The dressings require to be changed several times a day.

R. Werner confirms the non-irritant, prompt and intense anæsthetic action of cycloform. He was able to allay severe pain by means of the powder and the ointment. The ointment acts somewhat more slowly than the powder. He gives the following prescription for an ointment for wounds:

Rp. Cycloform	32.5 grammes (488 grains)
Naftalan	225.0 „ (7½ oz)
Lanolin anhydr.	175.0 „ (5⅝ oz)
Ol. oliv.	97.5 „ (3¼ oz)
Zinc. oxid.	100.0 „ (3⅓ oz)
Acid. boric.	50.0 „ (1⅔ oz)

### Diamido-anthraquinone sulphonic acid.

A new reaction for copper, which is very sensitive and particularly applicable to physiological and alimentary chemistry, is described by R. Uhlenhuth. As a reagent a solution of 1.2-diamido-anthraquinone-3-sulphonic acid



is used. It is prepared by dissolving 0.5 gramme of the acid in 500 c. c. of water, with the addition of 40 c. c. of solution of caustic soda (40° Bé.). With this reagent Uhlenhuth was

Zeller, *Medizinische Klinik* 1910, No. 45.

Werner, *Münchener medizinische Wochenschrift* 1910, No. 38.

Uhlenhuth, *Chemiker-Zeitung* 1910, No. 99, p. 887.



able to detect copper when the usual reagents failed. As a rule the fluid to be tested is poured into the reagent which assumes an intense blue colour in the presence of copper salts. The blue colour is still easily recognised in a fluid containing 1.9 parts of Cu in 1,000,000 parts. The limit is reached at 1.9:10,000,000.

### **Diaspirin.**

Diaspirin has proved an excellent diaphoretic in affections of the eyes, when it is required to free the iris from secretion and toxic substances by diaphoresis in conjunction with atropine treatment. In such cases it frequently happens that the usual remedies are unable to act on account of the well known action of atropine of preventing sweating. B. Sylla found that diaspirin did not fail in such cases, for being non-irritant the stomach is able to tolerate sufficiently large doses. The author gives the following directions for the treatment: At 6 p. m. the patient is given 1 gramme of diaspirin with a glass of water or warm lemonade. At 7.30 p.m. a hot foot bath is given, lasting 10 to 15 minutes. During this bath the patient takes another gramme of diaspirin and drinks 2 cups of hot elderberry tea with it. He is then put to bed wrapped in a woollen cover so that only the head is exposed. After 5 to 10 minutes profuse sweating commences, but if it fails another gramme of diaspirin is given half an hour later with hot tea. After the patient has sweated for an hour and a quarter, the covers are removed to allow him to cool. He then gets up, is washed with warm water and is given a light supper in bed. Warm compresses are applied to the eye for half to one hour longer, and 3 more drops of atropine and cocaine solution are instilled. In this way sweating is brought about by the author as a rule two evenings in succession, at the beginning of the acute illness and later every 5 or 6 days. This procedure was found by the author to lead to rapid subsidence of the symptoms, not only in acute iritis but also in other affections of the eyes, especially in conjunctivitis and oculomotor paresis and retrobulbar neuritis due to colds or influenza. Sylla also obtained

good results in other diseases such as corneal opacity, retinal hæmorrhage, exudative choroiditis, scleritis and episcleritis, and after inunction treatment to accelerate the elimination of mercury. As an analgesic diaspirin gave good results in ocular pain, in headache due to eserine, and in toothache. The dose for such cases is 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains).

J. Doberer used diaspirin with satisfactory results in several cases of gout. The remedy relieved the pain, reduced the inflammation and produced absorption. The author was unable to determine whether its diaphoretic properties assisted the action. In any case its action in gout is just as good as that of aspirin, and perhaps better. It has certainly the advantage over aspirin that it is tolerated better and produces more powerful diuresis, and this is certainly of importance in many cases.

## Digitalis Substances.

### *Folia digitalis.*

In an important communication on the treatment of epistaxis, Focke points out that spontaneous bleeding from the nose, of the kind common in chlorotic subjects, may be attributed to a local congestion dependent, as a rule, on a general circulatory disturbance. This disturbance must be combated, and the author regards it as one of the chief tasks of therapeutics to set it right, after the hæmorrhage has been checked by the usual methods, including cauterisation, plugging, cold compresses on the back of the neck, etc. The circulation is regulated first of all by suitable diet, relieving constipation when present, abstinence from coffee and stimulating foods and drinks in general, and by other obvious measures, whereupon medical treatment has to be resorted to. In the author's experience the best results have been obtained by the use of digitalis leaves in the form of an infusion. He considers a dose of 0.5 to 0.8 gramme ( $7\frac{1}{2}$ —12 grains) given in the course of two days sufficient to cure nasal bleeding in adults. These small doses never upset the healthy stomach. In at least three-quarters of the cases treated Focke saw no hæmorrhage after the

commencement of the digitalis treatment. Not only was the effect immediately evident, it was lasting, so that in many patients no bleeding recurred for weeks and months. In others it recurred after two years and yielded at once to digitalis. In many cases in which a subsequent operation is intended for the cure of the cause of bleeding, digitalis will also be of use. Focke reports several cases of swelling in chronic rhinitis and nasal obstruction by enlarged turbinals in which the hæmorrhage ceased at once after the use of digitalis. The surprising utility of digitalis is attributed by Focke to a relief of the disturbances of the circulation and the distribution of the blood, so that the venous and capillary congestion is abolished.

The continous use of digitalis in cardiac insufficiency is dealt with by V. Rubow. Toxic symptoms are readily produced in this case, and are dependent on the general constitution of the patients and on their sensitiveness to the toxic action of the drug. The author therefore suggests that digitalis should be given with suitable intervals, in such a way that there is no interference with the constant presence of digitalis in the body. He thus gave 0.1 to 0.125 gramme ( $1\frac{1}{2}$ —2 grains) of powdered digitalis leaves for 4 to 5 days, and then left an interval of 1 to 3 days. In this way the patients were kept continuously under the action of digitalis, whereas if longer intervals were allowed this would not be the case; and they remained free from toxic manifestations. In cardiac insufficiency due to nephritis somewhat smaller doses (0.08 gramme [ $1\frac{1}{4}$  grains]) are required, for in such cases digitalis is usually not well tolerated.

P. C. Franze obtained very satisfactory results in angina pectoris with a combination of digitalis with diuretics. He prescribes:

Rp. Fol. Digit. pulv.	0.1 gramme ( $1\frac{1}{2}$ grains)
Caffein.	0.2 „ (3 grains)
Diuretin.	0.5 „ ( $7\frac{1}{2}$ grains)
Morphin. hydrochl.	0.005 gramme ( $\frac{1}{12}$ grain)

M. Ft. pulv. Mitte V. Sig.: One powder to be taken during an attack, and if necessary another powder half an hour later.

Rubow, Hospitalstidende 1910, No. 1 and 2.

Franze, Folia therapeutica 1910, No. 2.



Quisling, in the treatment of croupous pneumonia, makes use of a combination of digitalis with camphor, for the latter stimulates the heart and acts on the vasomotor and respiratory centres. He gave during the first 12 hours 0.15 gramme ( $2\frac{1}{2}$  grains) of folia digitalis every hour in the form of an infusion, and 0.04 gramme ( $\frac{2}{3}$  grain) of camphor in the form of an emulsion.

With regard to the value of physiologically standardised digitalis leaves introduced during the last few years, J. Burman's experiments have not proved convincing. In his opinion the physiological standardisation of digitalis gives information merely as to the degree of toxicity, but not as to the curative action. Moreover the method is not free from objection, for frogs differ in their susceptibility to digitalis. Chemical investigation is more trustworthy, for by this means more reliable data may be obtained as to the amount of active substances present.

### Digipuratum.

In a further communication\*) on digipuratum, J. Szinnyei once more draws attention to the advantages of digipuratum treatment. In adjusting the doses of the preparation the author endeavoured to give it in such a way that the total daily amount was concentrated as far as possible in half a day. The patients were given not more than 0.5 gramme ( $7\frac{1}{2}$  grains) evenly distributed throughout the hours from midday to 9 p.m. As a rule the author prescribed 0.4 gramme (6 grains) on the first day, and modified the dose on the following day in accordance with the effect produced. Usually the patient was given 0.4 gramme (6 grains) on the first day and on each of the two following days, and subsequently 0.3, 0.2 or 0.1 gramme a day as required. In severe disturbances of compensation it is advisable to use energetic digipuratum treatment during the first three days, giving 0.4 to 0.5 gramme ( $6-7\frac{1}{2}$  grains) daily. By that time a well marked effect has set in, or compensation has been so far restored that the remedy

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Quisling, Tidschrift for den Norske Laegeforening 1910, No. 3.  
Burman, Schweizer Wochenschrift für Chemie und Pharmazie  
1910, p. 410.

\*) See Merck's Reports 1909, p. 179.

Szinnyei, Therapeutische Monatshefte 1910, No. 8 and 9.

may be left off, or, at any rate, the doses may be reduced to 0.1 gramme ( $1\frac{1}{2}$  grains). The smallest total amount required for a cure was found by Szinnyi to be 0.9 gramme (14 grains) the largest 3.2 grammes (48 grains); the average amount was between 1 and 2 grammes (15—30 grains). If the failure of compensation is actually threatening life, the treatment should be commenced by a cardiac remedy which can be applied intravenously, and digipuratum should be given at the same time.

W. F. Boos used digipuratum in 20 cases of failing compensation, among them some severe cases. He found the action of the preparation to be more rapid than is the case with other internal cardiac remedies. In many cases compensation was restored after 4 days. The author, as many others before him, lays stress on the fact that the remedy is always well tolerated without producing the least disturbance to the stomach or the intestines\*). Cumulative effects were never observed by the author, even in cases in which large doses had been given repeatedly. Similar results were obtained by C. Berri. E. Veiel, however, observed slight disturbances even after careful dosage, and in one case, that of a man of 44, after 5 tablets had been given within 4 days, he observed severe intoxication characterised by increased cyanosis, high tension pulse, a rise of systolic pressure and bradycardia. In comparing digipuratum with digitalis powder, Veiel found that both remedies had approximately equal power over the heart, though digipuratum is superior to digitalis powder in its action on diuresis. This result agrees with that reported by W. Smith of a patient aged 67 with arterio-sclerosis, failing compensation, hydrothorax, ascites and œdema, in this case digipuratum apparently had a very favourable effect. The patient had taken 4 tablets the first day, three on each of the second and third days and two on each of the following days. This treatment produced a definite increase in the amount of urine, and hand in hand with it the œdema disappeared and

Boos, Boston Medical and Surgical Journal 1910, No. 6.

\*) See G. Riebold, Münchener medizinische Wochenschrift 1910, No. 36. — Korrespondenzblatt des Vereins deutscher Ärzte, Reichenberg 1910, No. 10, p. 14.

Berri, Clinica medica italiana 1910, p. 465.

Veiel, Münchener medizinische Wochenschrift 1910, No. 39.

Smith, Boston Medical and Surgical Journal 1910, No. 6.

the cardiac activity improved. In so old a patient the action of the remedy is doubly striking. It is true the result is in part attributable to the diuretin treatment which was commenced on the third day of treatment.

An important addition to the indications for the use of digipuratum and of digitalis in general is reported by R. Tissot. He found that digitalis should be used in all cases in which the heart is badly nourished, where unusually heavy work is required of it, and where toxic substances are to be removed from the blood, for instance in pneumonia, bronchitis, bronchiolitis, diphtheria, influenza, puerperal infection, chlorosis, anæmia of unknown origin, articular rheumatism, erysipelas, and before operations, provided no narcotic drugs have been given. In pulmonary tuberculosis and in insufficiency of the liver it is best not to use digitalis. He directs that a single dose of caffeine (0.1 to 0.2 gramme [ $1\frac{1}{2}$ —3 grains]) be given before commencing the digitalis treatment. On the first day 0.1 gramme ( $1\frac{1}{2}$  grains) are given 4 four times a day, on the second day 0.1 gramme ( $1\frac{1}{2}$  grains) 3 times, on the third day 0.1 gramme ( $1\frac{1}{2}$  grains) twice, and on the fourth day 0.1 gramme ( $1\frac{1}{2}$  grains) once, so that on the whole 1 gramme (15 grains) of digipuratum is given, unless the action sets in so rapidly that a smaller total dose of 0.6—0.8 gramme (9—12 grains) is found sufficient. The action then as a rule continues for 10 to 14 days, during which time no digitalis whatever should be given. After this time the treatment may be repeated.

A paper on the pharmacology of digipuratum has been published by W. Hale. The author begins by confirming the finding that the preparation is an efficient digitalis remedy, and that the powder and the tablets have an equally good action. In a 10 p. c. solution it displays the same action as the official tincture and the commercial fluid extract. These results are completed by the communication of J. Franzen. The author showed in animal experiments that the administration of therapeutic doses did no harm to the stomach and intestines; toxic doses produced no

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Tissot, *Folia serologica* 1909, No. 1.

Hale, *Journal of the American Medical Association* 1910, No. 2.

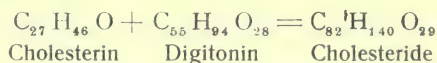
Franzen, *Dissertation Hanover* 1910.



change in the stomach, though they produced catarrh in the intestines. The dissection showed further that the kidneys were inflamed. These, and similar observations, point to the fact that the absorption of digipuratum takes place in the intestines, and that the stomach is left untouched. With regard to the possible occurrence of cumulative action after the use of digipuratum, the author has convinced himself that it may be prevented by appropriate dosage.

### Digitonin.

Crystallised digitonin, a digitalis glucoside, is insoluble in water, ether and chloroform, sparingly soluble in alcohol; it decomposes above 235° C. The preparation has no physiological action on the heart like other digitalis glucosides. It has therefore not been used therapeutically. The investigations of A. Windaus show that it may prove a very valuable substance in physiological chemistry, for its use enables a comparatively simple quantitative estimation of cholesterin. Windaus found that digitonin forms with cholesterin in alcoholic solution an addition product which is practically insoluble in alcohol (1 molecule of digitonin and 1 molecule of cholesterin).



For the quantitative estimation of cholesterin the material to be examined is dissolved in 50 times the amount of boiling 95 p.c. alcohol, and a 1 p.c. solution of digitonin in hot 90 p.c. alcohol is added, as long as a precipitate forms. After standing for several hours, the precipitate, consisting of digitonin cholesteride, is collected on a Gooch crucible, washed with alcohol and ether and dried at 100° C. The cholesterin is estimated from the weighed quantity of the precipitate by multiplying the amount of cholesteride by 0.25. Since the esters of cholesterin do not react with digitonin, the above described method may also be used for separating cholesterin from cholesterin esters. Further, the insolubility of digitonin cholesteride may be used for the qualitative demonstration of cholesterin, though this reaction

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Windaus, Zeitschrift für physiologische Chemie 1910, Vol. 65, p. 110.

See also Berichte der deutschen chemischen Gesellschaft, Berlin 1909, p. 238.

is not so sensitive as the more usual colour reactions for cholesterin.

### Digitoxin.

Crystallised digitoxin\*) has not even now received the attention it deserves in the internal treatment of cardiac troubles. This may be due principally to the sparing solubility of the preparation by reason of which it cannot be prescribed as a pure aqueous solution, as is the case with the infusion of digitalis. In other ways its properties are completely identical with those of digitalis both in respect of its action and secondary effects. Special interest therefore attaches to a comprehensive work by J. Corin in which his experiences, collected over a period of 15 years, are given regarding the value of digitoxin. A specially important result of Corin's observations is the good effect obtained by digitoxin in large doses in pneumonia. Digitoxin treatment should be commenced immediately the diagnosis is made, for in this way the disease may be cut short in the majority of cases if it has not fully broken out. In any case digitoxin has the effect of bringing about the crisis several days earlier. This effect may as a rule be obtained by a single comparatively large dose more readily than by repeated small doses. After giving the drug the author observed that the temperature soon fell. He lays more stress on the fact, however, that under the action of digitoxin the pulse very soon becomes fuller, slower and stronger. In his view the action of the drug depends on this effect, for by the rapid absorption of the pulmonary exudation the pneumococci are deprived of their nutrient medium. For this reason the remedy only displays a specific action in croupous pneumonia, while in broncho-pneumonia following measles this action is not produced. Again, in drunkards far less effect is obtained, and this has long been known to be the case with other digitalis substances. From the author's large collection of cases one case only will be described which showed the action of digitoxin in a very favourable light. In the case of his own child, 8 years of age, he gave 0.003 gramme ( $\frac{1}{20}$  grain) of digitoxin within 40 hours with

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\*) See Merck's Reports 1895, 1896, 1899, 1900, 1902 and 1904. Corin, *Le Scalpel et Liège Médical* 1910, p. 291, 315, 331.

the result that the pulse and temperature became completely normal on the third day. The author's cases show a mortality of only 5.4 p.c. in more than 600 patients. The mortality is rather higher in adults. If we exclude the patients with whom digitoxin did not agree, since they vomited immediately after taking it (6 cases out of 277), and one case which came under treatment in a moribund state, the death rate for adults works out at 9.5 p.c. The fact must be remembered, however, that about half of those who died were alcoholics. In 154 cases in which the beginning of the disease could be accurately determined, a cure took place in 3 days in 32 cases, 4 days in 52 cases, 5 days in 38 cases, 6 days in 21 cases and 7 days in 11 cases. The pulse and the temperature, however, returned to normal in a far shorter time in most of the cases. The results were so favourable that Corin is undoubtedly right in recommending the further trial of large single doses of digitoxin in place of its fractional administration. The most suitable method of prescribing it is given by the author as follows:

Rp. Digitoxin cryst. Merck	0.003 ( $\frac{1}{20}$ grain)
Chloroform	gutt. I—II (1—2 min.)
Alcohol	1 c. c. (17 min.)
Aq. destill.	50.0 ( $1\frac{2}{3}$ oz)
Vin. albi	
Syrup. capillor. Veneris aa	25.0 ( $\frac{5}{6}$ oz)

This mixture is given to an adult in a single dose at the beginning of the treatment, as cold as possible. Before taking it the patient should have had no food for at least an hour, and should be lying as flat as possible with the head slightly raised, and should take nothing to drink during the first hour after the treatment. If vomiting seems likely to occur, ice is placed over the region of the stomach. The emptier the stomach, the more rapid is the action of the digitoxin. If vomiting occurs after an hour the action is not usually diminished.

With regard to dosage\*) the following rule should be observed: An adult man is given at least 0.003 gramme ( $\frac{1}{20}$  grain) at the beginning of the illness. In rather more advanced cases with high fever, strong persons and alcoholics are

\*) The maximum dosage in common use for Digitoxin has been 0.001 gramme for a dose, and 0.003 gramme a day ( $\frac{1}{64}$  and  $\frac{1}{20}$  grain).



given 0.004 to 0.0045 gramme ( $\frac{1}{16}$ — $\frac{1}{15}$  grain), and occasionally 0.005 gramme ( $\frac{1}{12}$  grain) especially if no result is obtained 24 hours after the first dose. In children over 10 years of age, the dose at the beginning of the illness is at least 0.0025 gramme ( $\frac{1}{25}$  grain), in children under 1 year 0.0003 to 0.001 gramme ( $\frac{1}{200}$ — $\frac{1}{64}$  grain), and after pneumonia has broken out, 0.001 gramme ( $\frac{1}{64}$  grain) within 24 hours, or in a single dose. On the following days 0.0005 to 0.001 gramme ( $\frac{1}{120}$ — $\frac{1}{64}$  grain) are given. In children of 1 to 2 years a single dose of 0.001 gramme ( $\frac{1}{64}$  grain) is enough to begin with, though occasionally 0.0013 to 0.002 gramme ( $\frac{1}{50}$ — $\frac{1}{32}$  grain) are required within 12 to 24 hours. Between 2 and 3 years of age 0.001 to 0.0015 gramme ( $\frac{1}{64}$ — $\frac{1}{40}$  grain) are given at the beginning of the illness, within 24 hours, and after the disease has broken out, 0.0018 to 0.002 gramme ( $\frac{1}{35}$ — $\frac{1}{32}$  grain). Children of 5 to 10 years may be given pretty nearly the same dose as adult women. For the latter the author prescribes 0.0025 gramme ( $\frac{1}{25}$  grain), on an average, at the beginning of the illness.

The following conclusions are arrived at by Corin from his 15 years' experience: Digitoxin acts best at the beginning of pneumonia. By giving large doses it is possible to bring the disease to a standstill, provided it has not advanced too far, and the patient has not already become too severely poisoned. The action of digitoxin in pneumonia following measles is nil. It may be given with benefit even in this case, however, if the object be to strengthen the heart. It is not suitable, however, for the treatment of broncho-pneumonia consequent on measles. Like all cardiac tonics and most nervines, digitoxin is less effective in alcoholics.

### Dimethylglyoxime.

Tschugaeff found years ago that dimethylglyoxime formed with salts of nickel a compound of an intense red colour, and on this fact he based a very sensitive method of detecting this metal. A modification of this method is used by A. Bianchi and E. di Nola to detect small quantities

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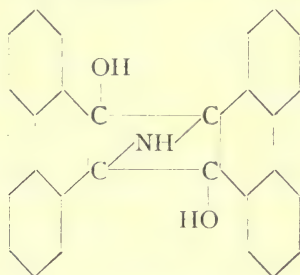
Tschugaeff, Merck's Reports 1905, p. 60.

Bianchi-Nola, Bollettino chimico farmaceutico 1910, p. 517.

of nickel in metals or other substances. Their method is to place the substance to be tested in a porcelain capsule and add two drops of concentrated hydrochloric acid or nitric acid. The solution thus obtained is neutralised with ammonia, and acidified with acetic acid, when a few drops of a saturated solution of dimethylglyoxime are added. In the presence of nickel a red colour appears at once. The reaction may be carried out either in the porcelain capsule or on filter paper. In the latter case the acid solution is poured on to the paper and the test is completed as described.

### Di-9-10-monoxypheanthryl-amine.

By heating 9-10-dioxypheanthrene with concentrated ammonia J. Schmidt and H. Lump p obtained di-9-10-monoxypheanthryl-amine, which forms a brown powder melting at  $385^{\circ}$  C. The compound is very sparingly soluble in the usual solvents, but it dissolves in concentrated sulphuric acid, the resulting solution has a blue colour. Its chemical formula is as follows:



The authors state, in a further publication, that this substance has been found a reliable and positive test for the detection of nitric acid or nitrates in the presence of other oxidizing substances, such as chlorates and chromates. This is a great advantage as compared with the many tests for nitric acid previously used. As a reagent a solution of 0.1 gramme of di-9-10-monoxypheanthryl-amine in 1 litre of pure concentrated sulphuric acid is prepared at ordinary temperature. If a solid substance is to be tested for nitric acid a grain of it is added to 2 to 3 c. c. of the reagent. In the presence of nitrates the pure blue colour of the reagent turns to a claret red. If a solution is to be tested, con-

Schmidt-Lump p, *Berichte der chemischen Gesellschaft Berlin* 1910, No. 5, p. 787 and 794.

centrated sulphuric acid is first added to it in suitable quantity, for the presence of water interferes with the reaction. For this reason the dry substance should always be used for the test whenever possible. While other oxidizing agents do not interfere with the reaction, nitrous acid or nitrites may give rise to error. Small quantities of nitrites do not alter the colour of the reagent, but larger quantities do so, presumably because they are in part oxidized to nitric acid, and then give the reaction.

### Dionin.

Last year\*) H. Schlesinger published a communication on the advantages of a dionin-scopolamine combination in the treatment of chronic painful diseases. In this paper he recommended the use of this combination in curing the morphine habit. Trials in this direction have in fact confirmed the utility of this combination. The author reported his results at a meeting of the Society for Internal Medicine and Diseases of Children in Vienna. He gave subjects of the morphine habit subcutaneous injections of a solution of 0.3 gramme (5 grains) of dionin, 0.00025 gramme ( $\frac{1}{250}$  grain) of scopolamine hydrobromide and 0.2 gramme (3 grains) of morphine hydrochloride in 10 gramme ( $\frac{1}{3}$  oz) of water. A syringeful (1 c.c.) was injected 2 to 4 times on the first day, and on the following days the doses were considerably reduced. On the third day the patient should receive not more than 0.02 to 0.03 gramme ( $\frac{1}{3}$ — $\frac{1}{2}$  grain) of morphine, and between the eighth to the twelfth day the morphine should be omitted altogether. Dionin and scopolamine may then be gradually left off one at a time without the appearance of symptoms due to abstinence. Dionin is less harmful than morphine, and is the best known substitute for morphine, as appears from a communication by Reif. He found that dionin never produces secondary effects, while morphine frequently gives rise to a dazed condition, nausea and vomiting. Dionin is of excellent service in ophthalmic practice, and this has frequently been mentioned in these Reports. Especially in cases in which energetic dilatation of the pupils is required, e. g., in traumatic catarrh

\*) See Merck's Reports 1909, p. 185.

Schlesinger, Deutsche medizinische Wochenschrift 1910, No. 1, p. 56.

Reif, Medizinische Klinik 1910, No. 9, p. 351.



and severe irido-cyclitis, the author strongly recommends the combined use of dionin and atropine. His method is as follows: a crystal of atropine is placed on the conjunctiva of the lower lid and is allowed to dissolve slowly, while the lachrymal sac is held closed. After exactly 7 minutes a little dionin — about the size of half a millet seed — is placed in the conjunctival sac, and is also allowed to dissolve while the lachrymal sac is kept closed. If the pupils are still capable of dilatation this occurs within a short time under this treatment. It certainly comes on more quickly and more certainly than following the instillation of dionin or atropine solutions. According to the author, this application of dionin and atropine may be repeated, for in young persons it is free from danger. In patients over 60 years of age, or in the presence of arterio-sclerosis, Reif does not use dionin. Dionin is also of special value in pleural pain and fractured ribs, for it appears to act very well on serous membranes. Similarly in inflammation of the pelvic peritoneum the author observed a prompt action following the administration of dionin suppositories (each containing 0.03 to 0.05 gramme [ $\frac{1}{2}$ — $\frac{3}{4}$  grain]). The fact that dionin does not cause constipation was brought out in these cases. This action on the serous membranes should be tested further.

E. Zirm reports his results with dionin in ophthalmic practice, and shows that in the course of time the preparation has become indispensable in eye work because of its many sided utility and its excellent action. Its invaluable services in producing absorption in exudation, in subacute and chronic affections of the eyes, particularly of the cornea and the iris, are probably regarded as indisputable by all ophthalmic surgeons. Zirm draws special attention to its utility in scrofulous ulcers and torpid infiltration of the cornea, in corneal opacity and retinal hæmorrhage, after cataract and other operations, in septic processes following operations, in traumatic erosions, etc. Good results were obtained by him with a combination of dionin and white precipitate ointment, calomel and subcutaneous injections of fibrolysin, in deep-seated corneal scars following parenchymatous keratitis. To procure absorption dionin is used as such in con-

centrated solution. Dilute solutions (1 to 2 p.c.) are of value on account of their analgesic action. Though superficial anæsthesia for ophthalmic purposes can be obtained by numerous remedies, Zirm considers dionin incomparably better than all other preparations as regards its local effect in relieving pain. This effect is particularly pronounced in the pain of glaucoma. It is well known that dionin increases the action of other remedies. For this reason a combination of eserine and pilocarpine with dionin was found successful both before and after iridectomy. The best effect from this treatment was obtained by the author in eyes with raised tension where practically nothing except enucleation could be done, or where the patients had become resigned and would not hear of any further operation. Blind glaucomatous eyes of this kind in the late stages or with staphyloma and increased tension were eased for long periods in many of Zirm's cases by the repeated use of the combined eye drops. For this purpose he prescribes 0.02 gramme ( $\frac{1}{3}$  grain) of pilocarpine hydrochloride, 0.03 gramme ( $\frac{1}{2}$  grain) of physostigmine salicylate and 0.2 gramme (3 grains) of dionin in 10 gramme ( $\frac{1}{3}$  oz) of water.

C. Adam also refers to the analgesic properties of dionin. He found it might be used with advantage in all painful diseases of the anterior part of the eye, also in scleritis and episcleritis, in which its action is said to be better than that of cocaine. In iritis the author considers that care is necessary, for in two cases of iritis with arteriosclerosis hæmorrhage followed the use of the remedy. It should be avoided generally in persons with bad blood vessels.

Selenkowski recommends dionin because of its analgesic effect and its power of getting rid of lymph in perforating wounds of the eyeball, in cataracts extruded into the anterior chamber after incising the lens capsule, in corneal ulcer with hypopyon, in detachment of the retina, iritis, irido-cyclitis and glaucoma. Dutoit reports a case of neuroparalytic keratitis, and considers that the only remedies that are likely to prove

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Adam, *Münchener medizinische Wochenschrift* 1910, No. 7. p. 358.

Selenkowski, *Wjestnik Ophthalmologie* 1910, No. 1.

Dutoit, *Korrespondenzblatt für Schweizer Ärzte* 1910, No. 26, p. 817.

successful when the cornea has lost its nutrition are such as increase the lymph stream and the circulation. For this reason he used dionin (in 1 and 5 p.c. solution) and he made the interesting observation that dionin actually caused a visible formation of numerous new vessels in the cornea, and thus promoted its regeneration. In the case fully described by him he attributes the good result to dionin, and recommends its use in similar cases.

The value of dionin and of dionin iodide has been favourably reported on by B. Sylla.

### Diplosal.

Schulze has found that in acute articular rheumatism diplosal always causes the rapid subsidence of the fever and of the other symptoms. Small doses of 0.5 gramme ( $7\frac{1}{2}$  grains) are not sufficient. In his experience the correct amount to give is 1 gramme (15 grains) 3 times a day. Still larger doses would no doubt agree well, though no better result would be obtained. The author was unable to prove a direct influence on the temperature, although the duration of the fever was shortened. Effusions in the joints, swelling and redness disappeared quickly on the use of diplosal; commencing endocarditis was checked and cured. A great advantage seemed to the author to lie in the fact that diplosal produced no sweating as occurs with sodium salicylate and aspirin. In chronic articular rheumatism no successful results were obtained with diplosal, although the pain abated, the joint changes were but little improved. Improvement was obtained in a case of pleurisy complicated with pericarditis. In such cases the action of diplosal is not so striking, although there was undoubtedly a diminution of pain. Very satisfactory results were also obtained by U. Silva with diplosal in acute articular rheumatism, and he found it of equal service in acute muscular rheumatism, myalgia, lumbago, endocarditis and pleurisy with effusion. The author observed no diaphoretic action, though the prep-

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Sylla, Wochenschrift für Therapie und Hygiene des Auges 1910, No. 19. See Merck's Reports 1909, p. 186.

Schulze, Fortschritte der Medizin 1909, No. 33.

Silva, Il Cesalpino 1910, No. 6. — Baltische pharmazeutische Monatshefte 1910, No. 5, p. 205. — Zentralblatt für innere Medizin 1910, p. 1125.



aration shows definite diuretic and antipyretic properties. Inflammation of the kidneys was never observed by Silva to follow the use of the remedy, although the urine was carefully examined in each case. He was able to prove, on the other hand, that it was absorbed fairly rapidly, and was in part eliminated in the urine half to one hour after it had been taken. A part of the drug appears to be retained in the organism; at any rate the author found that when 6 grammes (90 grains) were given daily, only 2 grammes (30 grains) were eliminated. No unpleasant secondary effects occurred in the 21 cases treated. This result is confirmed in A. Fried's communications. He used diplosal in acute articular rheumatism with equally favourable results as those of the other two authors. Another very favourable opinion on the therapeutic value of diplosal is furnished in a paper by P. Barbier who came to the following conclusions:

"Since the action of sodium salicylate depends solely on the salicylic acid which is liberated on the surface of the inflamed tissues, it would appear logical to use free salicylic acid as recommended by Stricker, the founder of salicylic treatment. Having regard to the sensitiveness of the digestive tract to salicylic acid it is preferable to use the substitutes for this acid (such as aspirin and diplosal) which are more readily tolerated, while they have the same action. Diplosal has the valuable advantage of remaining undecomposed until it reaches the intestine (hence it is tolerated exceedingly well by the digestive canal), further, it causes no profuse sweating like aspirin. For these reasons it is undoubtedly preferable to the latter. The effect of diplosal in acute cases of rheumatism may be said to be truly wonderful, both in its action and in the promptitude with which the latter sets in. With regard to the action of diplosal in chronic cases, though less energetic, it is still a valuable aid, and on the whole superior to earlier methods of treatment."

### Diuretin.

In the treatment of œdema in the subjects of arteriosclerosis, diuretin in combination with other remedies may

Fried, Wiener klinische Rundschau 1910, No. 25, p. 396.

Barbier, Folia therapeutica 1910, No. 1.

be of good service. L. Ph. Dmitrenko gives certain directions for this purpose, founded on the experience that the value of the diuretic properties of this remedy in arteriosclerosis may be increased by the vaso-dilator effect of the salicylic acid contained in diuretin. The author never observed inflammation of the kidneys after the use of the preparation, but he finds an inconvenience in diuretin, in that like theobromine, it occasionally causes nausea, which may increase to vomiting. These symptoms are also observed with the substitutes for diuretin, although in Dmitrenko's opinion they do not approach diuretin in efficacy. If diarrhoea is produced by the drug this may be successfully remedied by giving a gramme of subnitrate of bismuth 3 to 4 times. The following prescription is used:

Rp. Diuretin. 6.0—8.0 grammes (90—120 grs.)  
Infus. adonis vernalis 6.0—8.0:200.0 grammes (90 to  
120 grains in  $6\frac{2}{3}$  oz

or

Rp. Diuretin. 6.0 grammes (90 grains)  
Sod. nitrit. 0.6 gramme (9 grains)  
Infus. adonis vernalis 2.0:200.0 (30 grains in  $6\frac{2}{3}$  oz)  
Sig.: One tablespoonful every 2 hours.

or

Rp. Diuretin. 6.0 grammes (90 grains)  
Tinct. Strophanth. 2.0—4.0 (34—68 min.)  
Aq. destill. 200.0 ( $6\frac{2}{3}$  oz)  
One tablespoonful every 2 hours.

The last mixture is especially indicated if a rapid action on the heart is desired. If diuretin fails, theophylline or theocin may be tried, for in such cases the author has occasionally succeeded with these drugs. Euphyllin has not been found of use by him either internally or subcutaneously. Calomel is no doubt a good diuretic though its action usually requires a few days, after which it is more intense. The diuresis may then be kept up by diuretin.

### Enesol.

Enesol has been favourably reported on\*) in a contribution to the treatment of syphilis by C. Fränkel and

Dmitrenko, *Therapeutisches Oboshrenie* 1909, No. 17 and 18.

— *Münchener medizinische Wochenschrift* 1910, p. 1104.

\*) See Merck's Reports 1904, 1905 and 1906.

J. Kahn. The authors' statements show that the symptoms of constitutional syphilis disappear in a short time under the use of enesol, while broad condylomata and universal exanthemata are also beneficially influenced. Specific throat troubles, however, prove more obstinate. As compared with injections of corrosive sublimate, injections of enesol have the advantage of producing no secondary effects, such as inflammation of the gums, if these occur they are considerably milder, so that we are not compelled to abandon the treatment. Any signs in the gums are readily set right by painting them with a 5 p. c. solution of chromic acid. Occasionally patients complain of pain at the seat of the injection, but no hard, painful infiltration of the subcutaneous cellular tissue was observed in a single case after 50 injections. In the authors' opinion the enesol injections should be continued until a negative Wassermann's reaction is obtained. Even in cases in which this stage had not been reached by inunction treatment, the authors obtained a negative reaction after enesol injections. The desired result was usually obtained by a series of 30 to 50 injections of 1 to 2 c. c. of the commercial solution of enesol (in ampoules). We are not yet in a position to judge whether relapses are likely to occur. In comparing the inunction treatment with enesol treatment the authors found that in the same time the enesol injections led to a negative Wassermann's reaction in a larger percentage of cases than following the use of mercury ointment (55:42 p. c.)

G. Tregoeat also reports very favourably on the action of enesol in syphilis. Its content of arsenic makes it specially valuable in cases which have proved refractory to mercurial treatment. Enesol is said to be particularly well suited for the treatment of children and nervous patients, for the injections have little toxic action and are said to be painless. In malignant syphilis a more powerful preparation is required in order to obtain a prompt action.

R. Fleckseder tried enesol as well as dioxy-diamido-arsenobenzol in malaria. His results show that this tropical fever, in which quinine is frequently powerless to prevent a

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Fränkel-Kahn, Medizinische Klinik 1910, No. 7, p. 267.

Tregoeat, Annales de la policlinique de Paris 1909, November. —

Deutsche Medizinalzeitung 1910, p. 830.

Fleckseder, Wiener klinische Wochenschrift 1910, No. 36, p. 1279.



relapse, may be completely cured by the prolonged administration of enesol, injected into the glutei, the parasites made to disappear, and the result of the Wassermann reaction altered. Although dioxy-diamido-arsenobenzol produced a truly surprising effect in one case, a relapse occurred. In malaria the author has given altogether 20 intra-gluteal injections, each injection consisting of 2 c. c. of enesol solution, or in the course of 40 days a total of 0.46 gramme (7 grains) of mercury and 0.17 gramme ( $2\frac{1}{2}$  grains) of arsenic.

### Eucalyptol.

The value of eucalyptol in affections of the lungs and bronchi has again been described by M. Berliner. It is used in the form of intra-gluteal injections, as a rule, one injection of 5 c. c. (85 min.) of a mixture of 25 parts of eucalyptol and 75 parts of castor oil being applied every week. This treatment gave good results in chronic bronchitis, the patient improving both subjectively and objectively, especially in uncomplicated cases. It was also of good service in cases in which the patient's condition gave rise to anxiety by reason of intercurrent illnesses. Of course, other remedies and measures must be used at suitable moments. The author found that eucalyptol acted rather more energetically and promptly in young patients. The use of eucalyptol should be specially considered in gangrene of the lungs, and in tuberculosis. In the latter disease it aids the treatment, and it may be regarded as an actual curative agent in all stages, especially since it causes no unpleasant secondary effects and may be used in conjunction with other remedies. In place of the above mentioned eucalyptol mixture the author prefers a combination of menthol and eucalyptol. He first prescribes:

Rp. Menthol	10.0 grammes ( $\frac{1}{3}$ oz)
Eucalyptol	20.0 „ ( $\frac{2}{3}$ oz)
Ol. ricini	100.0 „ ( $3\frac{1}{3}$ oz)

Later he uses a solution of double this strength. Of the weaker solution he injects 2 c. c. (34 min.) 3 to 4 times every week, and later an equal amount of the stronger solution. The dose must be adjusted to suit individual cases.

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Berliner, Berliner klinische Wochenschrift 1910, No. 21. — See also Deutsche Ärzte-Zeitung 1904, No. 20 and 21.

### Eugallol.

In comparing chronic dermatoses with epithelial growths and chronic catarrh of the urethral mucous membrane, and their treatment by means of cutting and scraping instruments to remove excrescences, O. Ehrmann tried the use of reducing agents. His idea was founded on the fact that chronic epithelial growths in chronic proliferative catarrh are best dealt with by operative removal, and similarly the medicinal reduction of growths should be the best treatment in the cases under consideration. He used eugallol in his experiments in an aqueous or oily dilution (with castor oil), and applied it to the urethra by means of a brush. He observed the following special action of eugallol on the mucous membrane: 1. A superficial caustic action leading to the formation of a thin, white scab (epithelial opacity due to coagulation). 2. Painlessness of the area under treatment, or rather a short painful initial stage lasting a fraction of a minute followed by complete local insensitiveness at the place of application lasting a considerable time. (The author therefore calls the remedy a "caustic anæsthetic" or a "caustic mucous membrane anæsthetic" in opposition to the anæsthesia of purely peripheral neurotic origin produced by cocaine, and to the local anæsthesia produced by cold, when ethyl choride is used). 3. An action more nearly resembling the well known action of the preparation on the skin, leading to a reduction of the epithelial proliferation. This action is intense when a strong application is used (of pure eugallol), or mild when a weaker application is used (of eugallol with castor oil).

B. Kaufmann confirms the good effects of applications of eugallol. His best results were obtained in cases of chronic catarrh with thickening of the epithelium. In the presence of infiltration his results differed from some observations of Ehrmann in that he had no appreciable success. Improvement was also obtained in cases of gonorrhœa which had run their course, leaving no objective signs, but merely unpleasant sensations.

Ehrmann is led by his good results to recommend the use of eugallol in chronic proliferating catarrh, epithelial

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Ehrmann, *Therapeutische Monatshefte* 1910, No. 5, p. 230.

Kaufmann, *Therapeutische Monatshefte* 1910, No. 5, p. 235.

thickening and pachydermia of other mucous membranes, and he believes that indications for the use of the preparation will also be found in laryngological practice. In no case, however, should eugallol be regarded as a universal remedy for catarrh or gonorrhœa, for it is a remedy with a very specialised action on mucous membranes. Further experiments are required, not confined to urethral practice, to ascertain the possibilities of this preparation.

### Eumenol.

Under this name I have issued for the last 10 years a fluid extract from the root of a Chinese Araliacea known as Tang-kui. As already stated in these Reports\*) eumenol has been shown by the publications of F. Hirth, A. Müller, de Buck, G. Bufalini and H. Langes to give excellent results as an emmenagogue. Pharmacological tests have proved that it non-toxic and free from abortive action. Therapeutically it has been found to have a most favourable tonic action on menstruation, regulating retarded periods, increasing the amount of flow when deficient, and relieving pain, especially premenstrual pain. The above mentioned authors therefore consider it to be indicated in amenorrhœa and dysmenorrhœa, especially in dysmenorrhœa of purely nervous origin and in cases with no appreciable organic changes. The preparation is given 3 times a day in doses of a teaspoonful, while at the same time the other usual measures, such as massage, hydrotherapy, iron medication, etc., are adopted. Recently R. Palm has drawn attention once more to the value of eumenol. He has used it for 9 years in women with delayed menstruation, and has obtained satisfactory results. His report shows that eumenol was only used as an amenorrhœic to bring on retarded menstrual hæmorrhage. Unlike Müller he used no other therapeutic remedies. The result of the treatment could therefore be attributed to the eumenol.

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\*) Merck's Reports 1899, p. 69 and 1901, p. 80.

Hirth, Münchener medizinische Wochenschrift 1899, No. 23.

Müller, Münchener medizinische Wochenschrift 1899, No. 24.

de Buck, Belgique médicale 1899, No. 48.

Bufalini, Annali di Farmacoterapia 1900, p. 140.

Langes, Therapeutische Monatshefte 1901, p. 363.

Palm, Münchener medizinische Wochenschrift 1910, No. 1.



Mention can only be made of an interesting pharmacological work by E. Lezenius on the Tang-kui root, the drug from which eumenol is prepared, for its wide range of contents cannot be referred to briefly. I would merely remark that the author was led by his investigations to the conclusion that the Tang-kui root belongs to an umbelliferous plant very closely allied to *Levisticum officinale* Koch. He assumes that the root is obtained from the Japanese plant *Ligusticum acutilobum*. He was not able to prove this point, however, for lack of sufficient roots of this plant.

### **Eumydrin.**

Th. Pertik tried this substitute for atropine in pulmonary diseases, in order to study its value in the treatment of asthma. In general the remedy was found to be a useful substitute for atropine when given subcutaneously in combination with morphine. It never causes toxic symptoms though it appears frequently to interfere with the appetite. Disturbances of accommodation and acuity of vision occur later with it than with atropine. In a nervous anæmic patient, the origin of whose asthma could not be ascertained, it certainly was not a case of spasmodic asthma, the author was able to control the attacks successfully for a long time by means of eumydrin. In another case, however, in which a nasal polyp had been removed by operation, and bronchitis and emphysema were present, no benefit was obtained from its use. Even after the bronchitis had been relieved it was prescribed with no effect. In three phthisical patients the asthma was relieved by it for a time, and the author accordingly regards these cases as a proof of its symptomatic efficacy. As he observed asthma in very few cases of phthisis, or of neurasthenia, he believes that the attacks are not nervous, but that they are far more probably due to toxins as in cases of lead poisoning, uræmia and gout\*).

In place of Tucker's asthma cure, A. Goldschmidt

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Lezenius, *Pharmazeutische Zentralhalle* 1910, No. 12.

Pertik, *Gyogyaszat* 1910, No. 5.

\*) For the dosage of Eumydrin see Merck's Reports 1903, 1905, 1906 and 1907.

Goldschmidt, *Münchener medizinische Wochenschrift* 1910, No. 43.

recommends the following solution for inhalation with a spray:

Rp. Alypin. nitr.	0.3 gramme (5 grains)
Eumydrin	0.15 „ (2 $\frac{1}{3}$ grains)
Glycerin.	7.0 grammes (100 min.)
Aq. destill.	25.0 „ ( $\frac{5}{6}$ oz)
Ol. pini pumil. min.	I

For use, about 10 grammes ( $\frac{1}{3}$  oz) of this solution are placed in the spray, and 8 to 10 drops of adrenalin solution are added. It is not advisable to mix the two solutions previously, for the mixture soon decomposes.

### Euophen.

Pick considers euophen\*) to be an important remedy in ophthalmic practice in severe infective diseases, particularly when the usual therapeutic remedies prove insufficient. In a number of cases, especially of perforating wounds affecting the eyeball, the author obtained excellent results. His cases include injuries by glass or needles with traumatic cataracts, hypopyon, and purulent iritis. The author's treatment consisted in opening the eyeball, evacuating the pus and introducing euophen into the interior of the eye. By this treatment Pick was able to discharge, with fair vision, 3 patients whose vision had been regarded as lost. The author also found it useful in severe *ulcus serpens*, used in combination with the customary operative measures, including cauterization and incision of the cornea; the results being apparently better than those obtained by operation alone. Injurious secondary effects are not produced by the remedy.

### Extractum filicis liquidum.

E. de Renzi pointed out some time ago that extract of male fern might be used not only for tapeworms, but also for the cysticerci of various kinds of tapeworms which inhabit other parts of the body. The value of the preparation in this direction is confirmed by Dianoux, who used extract of male fern in a case of *cysticercus* of the vit-

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Pick, *Therapeutische Monatshefte* 1910, No. 4, p. 183.

\*) See Merck's Index 1910, p. 102.

Renzi, *Merck's Reports* 1908, p. 199.

Dianoux, *Klinisch-therapeutische Wochenschrift* 1910, p. 166.

reous. Various symptoms led the author to examine his patient's eye, where he found a fungus-like formation at one side of the eye, and in the middle he made out the movable head of a cysticercus. On giving a tæniacide, a tænia solium was discharged. As an operation would have exposed the patient to various dangers, he tried the use of extract of male fern. He gave 0.5 gramme ( $7\frac{1}{2}$  grains) of the extract 3 to 4 times a day in capsules, and found, after 2 weeks, that the cysticercus had lost its motility, and that the vesicle surrounding it had shrunk and become flat. After giving the extract at intervals for 70 days the parasite entirely disappeared. The epileptic attacks which had occurred at the beginning of the treatment left off during the course of treatment. Dianoux therefore assumed that a cysticercus was also present in the brain, and had also yielded to the treatment.

#### **Faex medicinalis.**

In order to study the bactericidal properties of yeast, and at the same time ascertain what substances possess this property, J. Tsuru carried out a number of experiments with beer yeast of various kinds, and came to the following conclusions: "In ordinary nutrient broth and with weak solutions of sugar, yeast cells have no inhibitory or bactericidal action on bacteria, for there is no fermentation in these cases. The bactericidal action of yeast depends on processes of fermentation, but does not show itself until these processes have reached a certain degree, or there is a particular amount of grape sugar, viz., 20 p. c. The fermenting fluid then exhibits a definite bactericidal action. The bactericidal action is really due to the products of fermentation. These act most powerfully when together (acids and alcohol). Separately the acids have a fairly powerful action, the alcohol a rather feeble action. The bactericidal action of yeast does not depend directly either on the zymase or on the endotrypsin of the yeast cells." These results may possibly explain successes and failures in the external use of yeast, as for instance in the treatment of vaginal infections. They may also indicate the manner in which sugar may best be used in this treatment.



O. Abraham has continued his experiments with yeast, and has published his results. His bacteriological investigations show that a bactericidal action can be obtained with yeast, and that the addition of sugar is only necessary if the yeast no longer contains any cells capable of multiplication. Sugar must therefore be added in using yeast that has been stored, or the expressed juices of yeast. He is of opinion, however, that the products of fermentation, alcohol and carbonic acid, are not responsible for the bactericidal action of yeast. Neither could the zymases or the proteolytic ferments be held responsible, for it is not certain that the action of yeast is due to a ferment. It is possible that the autophagy of yeast plays a part. Hence the nature of the bactericidal substances of yeast has not yet been fully cleared up. To overcome the difficulty of bringing yeast preparations into sufficiently close contact with the diseased mucous membrane, the author now uses a mixture of yeast, kaolin, sugar and nutrient salts sterilised in a particular manner. This is issued under the name of "Xerase powder or Xerase capsules" in the form of a powder and of capsules containing 3 grammes (45 grains) each. This preparation keeps well and is convenient for use. The kaolin gives it the property of imbibing water, and thus causing firm adhesion between the mucous membrane and the yeast. In this way the action is spread over a large surface, and is made to extend to some depth. Xerase capsules are applied to the vagina by inserting them in front of the os uteri through a speculum, and fixing them by a plug of wool. After 24 hours the wool is removed, the vagina is thoroughly cleansed and a new capsule is then inserted. If the mucous membrane is severely inflamed, xerase powder may be used. In colpitis the author has obtained lasting cures by the insertion of a few capsules, while erosions heal more slowly because the pseudo-erosion is first converted into a genuine erosion, and this does not heal until it has led to detachment of the squamous epithelium round its margins. Catarrh of the cervix and corpus are greatly benefited by this treatment, although the property of the cotton wool of absorbing pus may be a material factor.

With regard to the internal administration of yeast in acne, furunculosis and urticaria, R. Polland states that a successful result is only to be expected when the disease is related to the functions of the digestive apparatus. In this case, however, it may be regarded as a valuable aid to the external treatment.

### Fibrolysin.

The past year has again seen the publication of a number of important papers on the therapeutic use and the undoubted efficacy of fibrolysin in various joint affections and scar formations\*).

The mode of action of fibrolysin is made clear in a paper by E. Starkenstein. He finds that thiosinamin or fibrolysin possesses a definite action of furthering the conversion of collagen into gelatin, and the allyl group contained in this remedy may be regarded as its carrier. The author's experiments were all carried out at the temperature of the body so that the results may be applied to conditions existing in the organism. This may furnish an explanation of the softening of scar tissue observed to occur as the result of fibrolysin treatment.

In joint diseases with ankylosis, F. Heeger gave one injection daily. Each fibrolysin ampoule was first warmed to 45° C. so that the fluid should reach the organism at the temperature of the body. It was then injected into the glutei and produced no unpleasant secondary effects. The patients treated by the author came from various classes, were of diverse ages, and none received more than 20 fibrolysin injections. After the tenth injection they were treated with massage, medico-mechanical exercises, etc. The results were on the whole very satisfactory in chronic arthritis, coxitis, chronic articular rheumatism, arthritis deformans, and omarthrititis, and the author had not a single case in which there was not some effect on the disease, though the improvement might be slight in some cases. In all cases it

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Polland, Münchener medizinische Wochenschrift 1910, p. 1158.

\*) See Merck's Reports 1904—1909 and T. Schrom, Sammelreferat über Fibrolysin, Klinisch-therapeutische Wochenschrift 1910, No. 43, p. 1049.

Starkenstein, Therapeutische Monatshefte 1910, No. 2, p. 68.

Heeger, Münchener medizinische Wochenschrift 1910, No. 5, p. 244.

displayed a very good effect on the general condition, and no doubt the baths were in part responsible for this. Having regard to the fact that most of the author's patients had been subjected for years to other methods of treatment without result, fibrolysin has certainly shown itself to be a useful remedy, and superior to other preparations. The reports of A. P. Luff, L. Williams, E. Suñer and Ch. J. MacAlister agree on this point. Luff used fibrolysin in a number of cases of thickened fibrous tissue with fibrositis and arthritis (also in Dupuytren's contraction). In most cases good results were obtained, especially in cases of stiff joints in which the result was remarkable, for joints which had become practically useless were rendered freely movable in the majority of cases by fibrolysin treatment. Provided the fibrolysin is not used while there is still active trouble in the joint, we may reckon on a success in at least two-thirds of the cases treated. MacAlister also regards fibrolysin as a valuable remedy in patients in whom the joints have become stiff as the result of fibrous adhesions and thickening of the synovial and periarticular tissues. The treatment contributes to the restoration of movement to the joints. Williams describes a case of sciatica in which he applied fibrolysin injections above the sciatic nerve with the result that the patient was able to walk after 3 weeks. Suñer has observed good results from fibrolysin treatment not only in joint stiffening, but also in extensive scars consequent on burns and in congenital, spastic stiffening of joints in children. In hereditary spasmodic paralysis, again, he obtained an improvement in the muscular rigidity.

Hochsinger reports a case of synovitis which extended to the vertebral joint. A completely successful result was obtained after 3 weeks' treatment consisting of one fibrolysin injection a week. Favourable results are also reported by F. Brandenburg in a case of chronic progressive polyarthrititis in a girl of 14 years, a condition which

Luff, *Lancet* 1910, No. 4515, p. 712.

Williams, *Lancet* 1910, No. 4508, p. 240.

Suñer, *Clinica castellana* 1910, 15<sup>th</sup> July (Valladolid).

MacAlister, *British Medical Journal* 1910, No. 2588, p. 303.

Hochsinger, *Revue de thérapeutique* 1910, No. 15, p. 522.

Brandenburg, *Münchener medizinische Wochenschrift* 1910, No. 24, p. 1280.



is well known to be very difficult to influence by medical treatment. By using injections of fibrolysin he obtained such marked improvement that the patient, who had been bed-ridden for more than a year, was able to leave her bed and walk. J. Stargardter, however, in a similar case in a child of 10, observed neither a subjective nor objective improvement as the result of intra-gluteal injections of fibrolysin amounting altogether to 42 c.c.

With regard to the treatment of scars, J. Dillon recommends a trial of fibrolysin before proceeding to operation. In superficial scars we may always reckon on a positive result. In deep seated organs, too, as in strictures of the œsophagus, etc., fibrolysin has been long recognised to be very valuable. In the author's opinion, the remote action of the preparation on scars requires no further confirmation. Strictures form the special condition in which fibrolysin has given the most excellent results, and Walterhöfer shows this in a valuable collective reference to the literature on fibrolysin. Recently J. W. D. Megaw and H. C. Howard have alluded to this fact. Megaw used fibrolysin in a traumatic stricture of the œsophagus caused 10 months previously by drinking solution of caustic potash. For the last 3 months the patient had been able to take only fluid nourishment, and not more than a teaspoonful at a time. After 5 injections of fibrolysin given at intervals of 2 days the patient was able to take bread and milk, and a few days later eggs and bread and butter, no other treatment having been used during this time. In this case the action was just as definite as in the case reported by Howard. This was a case of a woman who had a hard, fibrous stricture of the rectum after an operation for hæmorrhoids. She was given 3 injections a week, whereupon the formation of fibrous tissue ceased, absorption occurred up to a certain point, and the pain subsided. Defæcation caused little or no pain.

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Stargardter, *Archiv für Kinderheilkunde* 1910, p. 164.

Dillon, *Russkij Wratsch* 1909, No. 43. — *Petersburger medizinische Wochenschrift* 1910, No. 30, p. 401.

Walterhöfer, *Deutsche medizinische Wochenschrift* 1910, No. 38, p. 1762.

Megaw, *Indian Medical Gazette* 1910, p. 191.

Howard, *Lancet* 1910, No. 4508, p. 240.

Bausenbach treated a patient who had been operated upon two years previously for typhilitis, with the result that adhesions had formed round the cæcum, and were causing continuous pain. After 20 injections of fibrolysin they disappeared, while the pain subsided after the third injection.

L. Fiori tried fibrolysin in some cases of Dupuytren's contraction. In a man of 72 he obtained obvious improvement, but the injections caused malaise and had to be left off. The same occurred in a man of 55 with valvular disease of the heart. A very satisfactory result was obtained, however, in another patient who showed a distinct improvement in his general condition after 10 injections, while the fibrous nodes on the palm of the hand disappeared for the greater part, and the fibrous fascicles disappeared entirely, so that the fingers were free to move once more.

Fibrolysin is of special value in scleroderma. In a case of this kind J. A. Raíces gave first an injection every 2 days, then one every 8 days, with the result that after 60 injections the patient was almost cured, the board-like skin over the thorax, abdomen and leg being considerably softened, so that it was readily folded, the folds of the groin and the respiratory movements were normal, and the patient was able to walk again. Three months after the termination of the fibrolysin treatment, the author was able to ascertain that the improvement had been maintained. Wolters and Ledermann have also described the good effect of fibrolysin in a case of scleroderma (with sclerodactylia).

A. Braga describes some cases of interstitial hepatitis in which fibrolysin in the form of rectal injections gave good results. Every other day 0.2 to 0.6 gramme were used with the result that the liver and spleen improved, and considerable diuresis was brought about. Schnitter gives a full account of this diuretic component of fibrolysin action.

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Bausenbach, *Medizinische Klinik* 1910, No. 49, p. 1941.

Fiori, *Riforma medica* 1910, 18<sup>th</sup> July.

Raíces, *Dissertation Buenos Ayres* 1910. — *La ciencia medica* (Buenos Ayres) 1910, No. 2140.

Wolters, *Korrespondenzblatt des Mecklenburgischen Ärzte-Vereins* 1910, No. 307.

Ledermann, *Berliner klinische Wochenschrift* 1910, p. 1993.

Braga, *Bollettino delle cliniche* 1910, p. 217.

Schnitter, *Münchener medizinische Wochenschrift* 1910, No. 19, p. 1008.

The author found that the diuretic effect extended over a long time, and after reaching its greatest intensity the daily quantity of urine sank very gradually, to the normal amount before the fibrolysin injection. This long-continued diuretic action produced by relatively small amounts of fibrolysin (2.3 c.c. = 1 ampoule divided and given in two days) is thought by Schnitter to be the chief value of the remedy, and he considers this of more importance than the actual maximum of diuresis obtained by an injection. At any rate it would be worth while to test fibrolysin in suitable cases for its power of increasing diuresis.

Excellent results in *tabes dorsalis* are reported by F. Lésin. In a woman of 58, who had had 5 still-born children and had suffered for 15 years from severe pains in the abdomen, gastric troubles with cramp, and vomiting and constipation, the author gave an injection of fibrolysin every 2 to 3 days. After 20 injections, which were well borne, the pains left off and the appetite increased. Further, she was able to walk considerably better, and her weight had increased by 12 pounds. A few months later the symptoms returned. Fibrolysin treatment again led to the subsidence of all the symptoms and to a striking improvement in the patient's condition. In another tabetic patient fibrolysin again gave excellent results.

The observations of Kolossow show the action of fibrolysin to be of special interest in diseases of women; there are as yet few reports on this subject. The author observed that after the use of fibrolysin the tissues of the vagina became extraordinarily flexible and juicy. He concludes that the preparation leads to a considerable increase in the capillary flow, and that the beneficial action of fibrolysin upon scars is due to an infiltration of the tissues with fluid. His experience includes endometritis, metritis, fixation of the uterus, version of the uterus and gonorrhœa with oöphoritis or salpingo-oöphoritis. In every case the pain left off after a few injections, the uterus became more mobile and could be returned to its normal position. Confirmation of the usefulness of fibrolysin in this direction is afforded in a paper by A. Sacchi who obtained very

Lésin (Bruxelles), Communicated in a letter.

Kolossow, *Wratschebnaja Gazetta* 1910, No. 6.

Sacchi, *La Ginecologia* 1910, 15<sup>th</sup> February.



satisfactory results in retroversion of the uterus by intra-gluteal injections of fibrolysin and plugging with ichthyol glycerin. He therefore considers it advisable to use fibrolysin treatment in all cases of retroversion of the uterus due to adhesions before proceeding to an operation, for in most cases fibrolysin rapidly renders the uterus movable by causing the cicatricial adhesions to soften. In his experience 4—20 injections are required.

A strikingly successful result was obtained by M. Thilliez in a case of profuse hæmorrhage in the vitreous. At the beginning of the fibrolysin treatment the patient's vision was so slight that he could not count fingers. After a few injections his vision had increased to one-sixth, and after a few months to two-thirds of the normal acuity. R. Presas, in a scar on the eye-lid caused by a burn, gave 20 fibrolysin injections with the result that the patient was once more able to close his eye.

In heart disease and in chronic aortitis, fibrolysin may have a good effect on the dyspnœa and albuminuria by lowering the blood pressure. G. Castelli therefore tried it in a child of 10 with a heart affection consequent on repeated attacks of articular rheumatism. The examination showed not only cardiac hypertrophy with arrhythmia and an accelerated pulse, but also swelling of the liver, œdema of the face and weakness of the feet. All the usual cardiac remedies such as digitalis, strophanthus and digalen had failed entirely. Fibrolysin injections, however, (one ampoule injected into the glutei every other day) produced, after 10 days, a subsidence of the palpitation and dyspnœa, and after 3 weeks the general condition had improved so much that the patient was able to walk considerable distances. The result is attributed by the author to the effect of the fibrolysin on the pericarditis which is an important factor in heart disease in children.

The contra-indications for fibrolysin treatment given by

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Thilliez, La clinique ophtalmologique 1910, 10<sup>th</sup> July. — Journal des sciences médicales de Lille 1910, 3<sup>rd</sup> Sept. — Revue de thérapeutique 1910, p. 750.

Presas, Oftalmologia 1910, No. 10.

Castelli, Rivista critica di clinica medica 1910, No. 11. — Klinisch-therapeutische Wochenschrift 1910, No. 15, p. 369.

S. Stocker include present or past inflammation, e. g., conjunctivitis and keratitis, and cases in which softening of scar tissue would set free encapsuled virulent pathogenic bacteria, as in pulmonary tuberculosis, malignant tumours, bone affections and scars in the gastro-intestinal canal. The author believes that the febrile symptoms that have occasionally been observed after fibrolysin injections are attributable to the renewed activity of encapsuled bacteria. His view is in accordance with the observations of R. Neisse in a case of pleuritic adhesions in which febrile symptoms appeared after a series of injections. Neisse assumes that this effect was due to the absorption of toxic products from the tuberculous foci of the pleura or the lungs, and he advises care in its use when tuberculosis is suspected. He considers that fibrolysin injections should be discontinued if the least disturbance is noticed. Similar advice is given by F. Hayn.

A new indication arising from the property of fibrolysin of softening scars has been found in the treatment of syphilis, before using the Ehrlich-Hata remedy. W. Friedländer was the first to suggest fibrolysin for dealing with the infiltration caused by salvarsan, and for facilitating the absorption of salvarsan. More recently Touton has drawn attention to the lymphogenous action of fibrolysin. In cases of syphilis in which relapses have occurred even after treatment with salvarsan he hopes, by preliminary treatment with fibrolysin, to enable salvarsan to act more thoroughly and to bring about the "therapia sterilisans magna". He bases this opinion on the assumption that the spirochætæ which are closely entangled in the folds of the connective tissue are beyond the destructive action of the salvarsan, but the lymphogenous action of fibrolysin causes the connective tissue to swell and loosen, thus making them succumb to the treatment, and preventing them from remaining to cause relapses. Therefore it would be necessary to inject

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Stocker, *Korrespondenzblatt für Schweizer Ärzte*, Vol. 39, No. 24.

— *Wiener klinische Wochenschrift* 1910, No. 10, p. 368.

Neiße, *Therapeutische Monatshefte* 1910, No. 5, p. 257.

Hayn, *Münchener medizinische Wochenschrift* 1910, No. 7, p. 350.

Friedländer, *Deutsche medizinische Wochenschrift* 1910, No. 48, p. 2272.

Touton, *Berliner klinische Wochenschrift* 1910, No. 50, p. 2292.

fibrolysin, not with salvarsan, but before giving the latter, so that its action may have set in before that of the salvarsan.

The value of fibrolysin in veterinary practice is illustrated in an important paper by A. Buchholz, in which the author describes all results that have been obtained with fibrolysin in this direction, including his own. His experiences and the results obtained at the Veterinary College of Dresden show fibrolysin to be of use: 1. In chronic thickening of the skin and subcutaneous tissue after cellulitis, wounds and contusions; 2. In thickening of the mucous membranes; 3. In chronic fibrous tendinitis; 4. In diseases of the joints, provided ossification of the fibrous tissues has not advanced too far; 5. In relapsing inflammation; 6. In pleuritic operations. Other conditions include corneal opacities and fibrous tumours. A successful result cannot be expected in the case of old standing distension of bone or malignant tumours. The author points out further that foci of supuration are fanned into activity by fibrolysin.

The rapid cure of a horse lamed by inflammation of the patella ligament is reported by J. Glaas. A single application sufficed to enable the animal to return to work after 3 days, free from lameness. The author points out that he was dealing with a light horse, and that the pathological condition was of recent origin.

### Filmaron.

Filmaron\*) is obtained from the rhizome of *aspidium filix mas*. Recent reports by M. Ardell, P. Barabaschi, V. Gandini and F. Stringari have shown it to give excellent results as an anthelmintic. These authors find that it is easily taken, hence it may be used in children. It expels tapeworms just as certainly as *extractum filicis*, and gives rise to no unpleasant symptoms or toxic effects. Ardell, who used filmaron with good effect in 15 cases, found the smallest effective dose to be 0.6 gramme. The normal dose for adults is stated by him to be 1 to 1.5 gramme.

Buchholz, Dissertation, Dresden 1910.

Glaas, Deutsche tierärztliche Wochenschrift 1910, No. 38.

\*) See Merck's Reports 1903—1907.

Ardell, Allmäna Svenska Läkartidning 1909, p. 271.

Barabaschi, Gazzetta degli ospedali e delle cliniche 1910, No. 86.

Gandini, La Pediatria 1910, p. 706.

Stringari, Italia sanitaria 1910, No. 6.



Stringari and Barabaschi found filmaron superior in efficacy to other remedies for tapeworm. A more detailed account of the use of the remedy has been given in former numbers of these Reports.

A. Cavazzani found filmaron suited by its harmless qualities for the expulsion of worms, particularly in consumptive and feeble persons who are liable to contract tapeworm by eating raw meat. The author carried out 17 tapeworm cures with excellent success.

Successful treatment with filmaron in dogs is reported by Chandet. In the case of one dog the author produced not only the expulsion of numerous ascarides, but also the cure of impetigo, while in another animal a *tænia cucumerina* was expelled.

### Fluoresceïn.

Fluoresceïn, a red substance, is soluble in alkalis, showing a strong fluorescence, and when reduced is transformed into fluorescin, a yellow substance, and this, under the influence of oxidising agents (including the oxygen of the air) is very readily reconverted into fluoresceïn. Pure fluorescin in alkaline solution shows no fluorescence provided it is absolutely free from fluoresceïn, and in commercial specimens this can rarely be the case for well known reasons. The properties of the two substances led C. Fleig to devise a reagent the use and reliability of which put one in mind of the reagent recommended years ago by Meyer and Utz as a test for blood or oxidases. The reagent, which is intended to serve for the detection of blood in urine and other fluids, is prepared as follows; 0.25 gramme of fluoresceïn and 20 grammes of potassium hydroxide are dissolved in 100 c. c. of water, 10 grammes of powdered zinc are added and the mixture is heated to boiling. After clearing, the yellowish fluid thus obtained must be entirely free from fluorescence,

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Cavazzani, *Rivista critica di clinica medica* 1910, No. 38.

Chandet, *Schweizer Archiv für Tierheilkunde*, Vol. 51. — *Deutsche Tierärztliche Wochenschrift* 1910, No. 45, p. 674.

Fleig, *Presse médicale d'Egypte* 1910, No. 15, p. 281.

Meyer, see *Merck's Reagenzien-Verzeichnis* 1908, p. 175 and *Merck's Reports* 1903, p. 149.

Utz, see *Merck's Reagenzien-Verzeichnis* 1908, p. 263 and *Merck's Reports* 1903, p. 149.

otherwise it must be boiled again for a minute. It is then filtered, the reagent is placed in an amber-tinted glass bottle and is stored in the dark. It keeps better if about 2 grammes of powdered zinc are added. If it shows a slight fluorescence in the course of time, this disappears immediately when it is shaken. To carry out the reaction 2 c. c. of the urine to be tested are mixed with 0.25 c. c. of the reagent, and 3 drops of hydrogen peroxide (3 p. c.). If the urine contains blood an intense fluorescence appears at once, and this is obtained even when the test solution is greatly diluted, especially when it is observed by reflected light against a dark background. This reaction is said to be far more sensitive than that of Meyer (with phenolphthalin). Like most reactions of the kind, this one is only absolutely trustworthy when the result is negative.

### **Gelatina sterilisata.**

The action of gelatin on the coagulability of the blood has been carefully studied by H. Grau. By injecting 25 to 40 c. c. of 10 p. c. Merck's sterilised gelatin he obtained an increase in the coagulability of the blood that appeared on an average 2 to 4 hours after the application. At first it lasted only a quarter to half a minute, though from hour to hour it increased until 10 to 12 hours after the injection it had reached its maximum. The degree of increased coagulability varied in different experiments. The time of clotting usually declined by fully 66 p. c. and in isolated cases it declined as much as 85 p. c. This effect continued unabated for several hours. An explanation of the action of gelatin is still difficult to give. Grau thinks we can assume that we are dealing with an alteration in the concentration or in the molecular composition of the blood such as v. d. Velden postulated for explaining the action of the intravenous or stomachal administration of common salt. His investigations have shown that certain relations exist between the change of coagulability and the signs of reaction which frequently occur after gelatin injections. He concludes that we have to deal with conditions which depend on the sensitiveness of the body to the introduction of foreign substances

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Grau, Deutsche medizinische Wochenschrift 1910, No. 27.

v. d. Velden, Archiv für experimentelle Pathologie und Pharmakologie, Vol. 61, p. 37.

which resemble albumin. The practical importance of Grau's investigations lies in the confirmation of the fact that gelatin does actually deserve its reputation, and that it does materially increase the coagulability of the blood. The same result was obtained in the animal experiments carried out by J. Renard. He made the additional discovery that after an injection of gelatin the amount of fibrin ferment in the blood was increased for a considerable time, and further that as a rule the transitory, somewhat severe decrease in the number of white blood corpuscles gave place to a considerable degree of hyperleucocytosis. The author justly attributes the varying opinions as to the value of gelatin treatment to improperly prepared and sterilised solutions of gelatin. W. Engelmann for this reason uses "Merck's reliable preparation" for the treatment of *melæna neonatorum*, this preparation offering the best guarantee of freedom from tetanus germs. The gelatin solution is warmed to the body temperature, and 10 c. c. are injected by means of a syringe that has previously been well warmed. The injection is made into the subcutaneous tissues of the thigh, the skin being raised for the purpose. The same quantity is injected into the corresponding part of the opposite thigh. The punctures are covered with iodoform gauze and adhesive plaster. The tumour-like swellings of the subcutaneous connective tissue are treated with warm moist compresses to aid absorption. This part of the body appears more suitable for the injection than the intraclavicular region recommended by others, or both sides of the back, for the patient usually lies on his back, and the injections are least inconvenient in the thighs. The author illustrates the good effect of gelatin injections by quoting a case of *melæna*. Vassmer also obtained very satisfactory results with gelatin treatment in *melæna neonatorum*. His results show that without gelatin injections the mortality in 31 cases was 61·3 p. c., while when gelatin was used, of 34 cases only 8·8 p. c. ended fatally.

J. Zilz showed that gelatin injections yielded good

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Renard, *Russkij Wratsch* 1910, No. 11.

Engelmann, *Deutsche medizinische Wochenschrift* 1910, No. 24.

Vassmer, *Zentralblatt für Gynäkologie* 1910, No. 24.

Zilz, *Österreichische Zeitschrift für Stomatologie* 1910, No. 6.

— *Korrespondenzblatt des Vereins deutscher Ärzte von Reichenberg und Umgebung* 1910, No. 8.



effects in hæmophilia after the extraction of teeth. In 2 cases of severe hæmorrhage he placed stypticin tampons soaked in a hot gelatin solution in the bleeding part, and injected 40 grammes of gelatin subcutaneously, in the other case this dose was repeated an hour later, and another dose of 20 grammes was given on the following day; the 100 grammes of gelatin solution were borne without giving rise to symptoms of anaphylaxis or other sequelæ. In both cases the hæmorrhage was checked permanently.

H. Arnsperger also recommends intramuscular injections of sterile gelatin (20 c. c.) in addition to stypticin and hydrastis in hæmorrhagic diathesis. In this connection Brühl considers the subcutaneous injection of gelatin preferable, as a rule, for the practitioner to the intravenous infusion of common salt recommended by others for the treatment of internal hæmorrhage. In his opinion the subcutaneous use of Merck's gelatina sterilisata is convenient and safe, while it seldom fails even in the most obstinate hæmorrhage. Its value is not sufficiently recognised even now.

A contra-indication to the use of gelatin is stated by J. Studzinski to be parenchymatous renal hæmorrhage. In this case the author observed an increase in the hæmorrhage after the injection, while in chronic affections of the kidneys without hæmorrhage no appreciable harm was observed to follow the injections.

A new method of treating catarrh of the large intestine has been tried by L. v. Aldor in a number of cases. It consists in pouring hot gelatin solution into the bowel. His reports deal almost exclusively with severe forms of chronic catarrh of the large intestine, forming a transition to dysentery. An indication of the value of gelatin is provided by the fact that in the case described by the author the usual treatment had been used without success. The daily

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Arnsperger, Deutsche medizinische Wochenschrift 1910, No. 24, p. 1113.

Brühl, Internationales Zentralblatt für die gesamte Tuberkulose-Forschung 1910, No. 3, p. 137.

Studzinski, Przegląd lekarski 1910, No. 12. — Russkij Wratsch 1910, No. 4.

Aldor, Therapeutische Monatshefte 1910, No. 4, p. 171.

introduction of 40—80 grammes of sterile gelatin in 400 to 500 c. c. of Carlsbad water (at 45° C.) led in almost every case to a striking improvement which showed itself not only in the subsidence of the subjective symptoms, and in a reduction in the number of stools and an alteration in their consistency, but also occasionally in the functional activity of the bowel and in the endoscopic examination. The introduction into the bowel of hot gelatin solution is quite free from danger and produces no secondary effects.

### Globularin.

Globularin is a glucoside obtained from the leaves of *Globularia alypum* and *Globularia vulgaris*. It is a brownish-yellow powder, soluble in water and alcohol. Therapeutically it is used as a substitute for caffeine in cardiac and nervous troubles. It has usually been used in combination with globularetin, a side product of globularin, in rheumatism, gout, typhoid fever and Bright's disease\*).

Löwy states that trials in Jaksch's Clinic in Prague have shown that globularin stimulates the vaso-constrictors of the arteries of the kidneys. The local ischæmia thus brought about leads to a rise of blood pressure and transitory oliguria in normal persons. In diabetes the preparation leads to a long-continued diminution in the quantity of urine. Therapeutically this glucoside should be used only in slight cases of diabetes in which there is no excretion of acetone or aceto-acetic acid in the urine, and in diabetes insipidus. Löwy gave 0.1 gramme of globularin in 100 c. c. of water daily. He points out particularly that extensive trials and a large amount of material must be collected, and detailed observations made in order to decide the therapeutic value of the preparation. Jaksch, after giving 0.3 gramme of globularin to a patient with diabetes insipidus, observed a fall in the quantity of urine from 15 to 10 litres. In diabetes mellitus he also found that the quantity of urine fell from 7 to 2 litres after the use of the remedy, and in another case from 8 to 4 litres. The glycosuria is not affected by it,

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\*) See Merck's Index 1910, p. 136.

Löwy, Communication received from the author. — Prager medizinische Wochenschrift 1910, No. 50.

Jaksch, Revue de thérapeutique 1910, No. 17, p. 596.

neither does it increase the tolerance of the organism to carbohydrates.

### Glucose.

Glucose has been prepared for many years in sufficient purity to allow of its extensive use for nutritive purposes, in a natural manner and in other ways. It has been used with success in stomach troubles. W. Kausch and Berendes have now made use of glucose for subcutaneous and intravenous nutrition. Berendes uses 5 to 7 p.c. solutions for this purpose; one litre corresponds to about 200 to 300 calories. If the infusion of glucose is carried out several days in succession, a very slight excretion of sugar is gradually set up which may rise to 5 p.c. of the sugar introduced. The infusions do no harm, and give rise to no more trouble than the infusion of common salt. Kausch found it best to begin with one litre of a 5 p.c. solution, and to increase the concentration gradually, or to repeat the infusion twice a day, or even more often. For intravenous infusion a filtered and boiled solution of glucose in normal saline solution is used. To this may be added 4 to 8 drops of adrenalin per litre, if required. The subcutaneous injection is said to be less agreeable than the intravenous, while the latter has the advantage of enabling far larger quantities to be introduced. Another important observation of the author is the fact that the patient tolerates more glucose the lower the state of his nutrition is at the moment, and the poorer his condition in general. This applies both to the concentration of the solution and to the total quantity. The more miserable the patient is in any case, the more surprising is the enlivening action of the sugar infusions. In Kausch's opinion the infused grape sugar is used up in the organism. It certainly acts as a fuel material. Other remedies which enable the same number of calories to be given to a patient intravenously for a long time without pain have not yet been discovered by the authors. Cane sugar is also tolerated, but it is not consumed so completely, for the greater part of it is excreted again in the urine. The good results obtained by the authors in surgical cases led them to assume

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Kausch, Deutsche medizinische Wochenschrift 1911, p. 8.

Berendes, Zentralblatt für Chirurgie 1910, p. 1217.



that grape sugar nutrition must be suitable for other than surgical cases. They suggest the use of the method in severe vomiting in hysteria, hyperemesis gravidarum, in severe gastric and intestinal catarrh, and in other diseases which lead to the impoverishment of the body in fluid and nutritive substances, as for instance in Asiatic cholera.

### Glycerin.

Investigations into the cause of bothriocephalus anæmia some years ago led E. St. Faust and T. W. Tallquist to the result that this anæmia was caused by a hæmolytic lipid substance contained in the proglottides of the tapeworm. In pernicious anæmia, again, a lipid substance could be demonstrated in the stomach and intestines. The authors have now succeeded in showing that the hæmolytic substance is oleic acid\*), and they expressed the opinion that pernicious anæmia might be treated by abolishing the oleic acid in the stomach or by rendering it innocuous. Lime and glycerin are said to be suitable remedies for this purpose, especially the latter, for it forms with oleic acid triolein which is harmless. This theoretical suggestion takes for granted that the oleic acid glyceride does not become saponified in the alkaline intestinal juice. Whether the theoretical suggestions agree with facts or not, H. J. Vetlesen was led by the above investigations to make use of it in practice with strikingly good results, which certainly go to recommend his innocuous method for further trial. In a severe case of pernicious anæmia the author used no other treatment than the administration of a tablespoonful of glycerin 3 times a day, with the result that the hæmoglobin in the blood increased threefold, and the red blood corpuscles fourfold. This result led the author to assume that the favourable effect of bone marrow observed by Dixon Mann (and others) was attributable to the glycerin used in the extraction of the

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Faust-Tallquist, Archiv für experimentelle Pathologie und Therapie 1907, Vol. 57, p. 366.

\*) See E. Grafe, Münchener medizinische Wochenschrift 1910, No. 38.

Vetlesen, Norsk Magazin for Lægevidenskaben 1908, No. 12.

Vetlesen, Norsk Magazin for Lægevidenskaben 1909, No. 10. — Nordisches medizinisches Archiv 1910, Vol. 43, II. Part 2, No. 5, p. 21.

Dixon Mann, Merck's Reports 1908, p. 74.

marrow. Though this may be partly true, it is necessary to point out that most authors have used bone marrow with equally good results without glycerin. It is quite possible, however, that glycerin increases the efficacy of marrow. In a second communication which shows that the author was completely successful with the administration of glycerin, he states that the glycerin was given with lemon juice.

L. Preti tried glycerin in anguillulosis for the reason that the preparation is known to be capable of killing the larvæ of parasites. The remedy was given by mouth and by rectum, 25 grammes ( $\frac{2}{3}$  oz) of glycerin in gelatin capsules being given internally, and 2 hours later 30 grammes ( $\frac{5}{6}$  oz) by rectum. The capsules are intended to prevent a too rapid absorption of the glycerin, and also to enable the drug to reach the parts affected with parasites. This treatment is repeated twice a week. On the following day the fæces were found to contain numerous larvæ, mostly non-motile. After the second administration the number of larvæ expelled was considerably reduced, and after the third only a few larvæ could be found. Subsequent examinations revealed no larvæ. With the disappearance of the larvæ the patient's condition returned to normal. Glycerin should therefore be tried in anguillulosis, especially as the anguillula larvæ appear to be unaffected by extractum filicis.

### Gomenol.

Under the name of gomenol an essential oil prepared from the leaves of *Melaleuca viridiflora* (Myrtaceæ), of New Caledonia has been issued for some years. It is also called Niaoul oil (oleum Niaouli). Its chemical composition and its physical properties show that it is nearly allied to oil of cajuput. As previously stated in these Reports (Merck's Reports 1900) gomenol has been used in tuberculosis, bronchitis and pertussis on account of its power of diminishing secretion. Recently the preparation has been brought more to the front by a publication on its therapeutic value. Rallier du Baty has recommended it in place of iodoform-ether and naphthol-camphor for injection into tuberculous abscesses, for it is said to be less painful and less dangerous than the

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Petri, Therapeutische Monatshefte 1910, No. 2, p. 63.

du Baty, Gazette des hôpitaux 1909, 9th December. — Münchener medizinische Wochenschrift 1910, No. 14, p. 775.

other two remedies, while it acts better. The author commenced by injecting 5 to 10 drops, but then increased the dose rapidly. The tuberculous swelling is absorbed with satisfactory promptitude, a somewhat severe reaction being produced at the beginning of the treatment, marked by swelling of the tumour, pain and surrounding œdema. Baty used pure gomenol, though it is probable that it might be used with success suitably diluted with olive oil, if the reaction is found to be unduly severe and painful.

Favourable results with gomenol in whooping-cough are reported by P. Rousseau. The best results appear to be obtained by the subcutaneous and intravenous application of a 20 p. c. solution of gomenol in oil. Children of 2 years are given 3 to 5 c. c. (50—85 min.), children of 3 years 5 to 8 c. c. (85—136 min.), and older children 10 to 15 c. c. ( $\frac{1}{3}$ — $\frac{1}{2}$  oz). To avoid the pain produced by large doses the author recommends the application of moist dressings to the site of the injections. In small children the oil may be given intragluteally, in adults rectally. For rectal use a 33 to 50 p. c. mixture of gomenol and olive oil is given.

Brimont gives gomenol in combination with chloroform and castor oil in ankylostomiasis, preceded by a purgative in case of constipation. He prescribes the following mixture:

Rp. Ol. Niaouli	4.0 grammes (68 min.)
Chloroform.	3.0 „ (34 min.)
Ol. Ricin.	40.0 „ ( $1\frac{1}{3}$ oz)

The results of this treatment are encouraging, and further trials should be made.

Houdard found a mixture of tincture of iodine and gomenol (so-called iodo-gomenol) in every proportion to possess the full therapeutic action of the corresponding tincture of iodine, without its unpleasant irritant effects on the skin. He therefore recommends this mixture for disinfecting the hands of surgeons and the skin of patients, especially in minor surgery. Iodo-gomenol is also said to keep better than tincture of iodine.

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Rousseau, *Klinisch-therapeutische Wochenschrift* 1910, p. 1188.

Brimont, *Presse médicale* 1910, No. 85, p. 800.

Houdard, *Presse médicale* 1910, No. 85, p. 800.



### Gonosan.

In a report on the use of gonosan in gonorrhœa and cystitis, H. I. Berger comes to the following conclusions, completing and confirming earlier reports\*) as to the value of gonosan:

In every case of inflammation of the mucous membranes of the uro-genital tract where a disinfectant, bactericidal, astringent and analgesic remedy is indicated, gonosan fulfils all requirements, for its constituents are eliminated by the urinary passages and consequently come into contact with the diseased region. Even when its use is continued for a long time no unpleasant secondary effects are observed. Thanks to the analgesic action of Kawa-Kawa on the gastric mucous membrane, one very seldom observes nausea, vomiting or eructation. In every case of cystitis, which is usually caused by infection by micro-organisms, gonosan exerts its antiseptic and bactericidal action, and holds in check the processes of decomposition and suppuration. Hence gonosan changes the condition of the urine in a few days by causing the disappearance of the pus, phosphates and bacteria. The sedative properties of gonosan are apparent by relieving the following pains: the suprapubic bladder pain, the burning pain and straining on micturition, the pain at the caput penis due to inflammation of the bladder and the perineal and spermatic pain due to the same cause. Simultaneous disease of the kidneys forms no contra-indication to the use of gonosan as in the case of other essential oils, for the reason that the preparation does not irritate the kidneys. The administration of gonosan may be begun at any stage of gonorrhœa, though its action is more certain the earlier it is used. If it is prescribed on the appearance of the first signs of urethritis, a cure is rapidly obtained, and complications are less apt to occur. Suppuration in the kidney, in the bladder and in the urethra may be checked to some extent by the continued use of gonosan. Gonosan acts best when the urinary tract is clean, and for this reason it is of advantage to give a mild non-irritant diuretic at the same time. In atony and paralysis of the bladder, the bladder must be washed out. In gon-

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Berger, Deutsche Medizinal-Zeitung 1910, No. 2, p. 35.

\*) Merck's Reports 1902—1909.

orrhœal cystitis and in specific urethritis gonosan checks the development of the growth of Neisser's gonococci.

In recent acute gonorrhœa, L. Waelsch regards gonosan as the best balsam, especially when there is severe periurethral infiltration, and possibly lymphangitis, œdema of the foreskin and severe subjective pain forming a contra-indication to immediate local treatment. In such cases it gives specially good results by reducing the subjective troubles and diminishing the amount of discharge.

G. Joachim points out that the substitutes on the market do not give the same results as gonosan, for the raw products used in the substitutes do not correspond to the components of gonosan.

### Guaiacol preparations.

The great value of guaiacol and creosote preparations in pulmonary tuberculosis has been pointed out once more by K. Martin. Among other preparations he largely prescribes guaiacol carbonate, guaiacose and creosotal. Guaiacol carbonate is said to give very good results, especially in combination with myrrh and balsam of Peru in the form of pills. The author's prescription is as follows:

Rp. Guaiacol. carbon.

Balsam. Peruvian.

Myrrhæ pulv. aa 2.0 grammes (30 grains)

M. Ft. pil. L.

Sig.: 2 pills to be taken 3 times a day, half  
an hour after meals.

In most cases the author found this remedy to lead to an improvement in the subjective and objective condition. Thus, where there was loss of appetite, a strong desire for food set in, the strength and weight increased gradually, cough and phlegm ceased, the phlegm altered in appearance, or ceased altogether, the shortness of breath improved, night sweats left off, etc. There was a corresponding improvement in the condition of the lungs, the râles diminished or left off, dull areas became resonant, and in cases that were not too far advanced the signs of disease completely dis-

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Waelsch, Prager medizinische Wochenschrift 1909, No. 39.

Joachim, Medizinische Klinik 1910, No. 15.

Martin, Fortschritte der Medizin 1910, No. 32.

appeared. The common view that the action of creosote and guaiacol preparations depends on the increase in appetite and on the resulting gain in weight and in strength does not altogether appeal to the author. He believes rather that the action of the remedy goes farther, that in addition to improving the general condition it has a direct influence on the lungs. He supports his view by pointing out the improvement in the physical signs in the lungs, and in the phlegm, even in cases in which there is no gain in appetite or in strength. Hence the drug must have a specific action on pulmonary tuberculosis. The action of guaiacol carbonate on the intestine is easier to explain, for guaiacol is liberated and exerts its powerful antiseptic action. For this reason it is particularly well suited as an intestinal antiseptic in infective diseases. Liaschenko prescribed guaiacol carbonate with excellent results in chronic enteritis in children with intestinal putrefaction. As a rule he gave a dose 3 times a day. Children of 2 years were given 0.1 gramme ( $1\frac{1}{2}$  grains) for a dose within 24 hours, children of 2 to 10 were given 0.15 to 0.2 gramme ( $2\frac{1}{3}$ —3 grains) every 3 hours, or as much as 1 gramme (15 grains) a day. Infants were given 0.05 gramme ( $\frac{3}{4}$  grain) 3 times a day in combination with a tannin preparation (tannalbin). Guaiacol carbonate is contra-indicated in all acute gastro-intestinal affections accompanied by vomiting, gastric and abdominal pain and liquid stools.

R. Burow treated tuberculosis with a combination of sodium guaiacolate and potassium guaiacolate (3:100), to which 0.01 p. c. of arsenic was added. He was thus using solutions containing 1.5 gramme (24 grains) each of sodium and potassium guaiacolate and 1 gramme (17 min.) of liquor arsenicalis in 100 grammes ( $3\frac{1}{3}$  oz) of water. In experiments on animals it was found that the internal administration of this mixture for 4 weeks caused an increase of weight and an increase of hæmoglobin in the blood, with enhanced appetite, and increased diuresis. The author ascertained moreover that tubercle bacilli in glycerin agar cultures are not inhibited in their growth by guaiacol salts, but that arsenious acid by itself, as well as in combination with guaiacol salts, has a bactericidal action. Further, the blood serum

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Liaschenko, *Semaine médicale* 1910, p. 370. — *Praktitscheskij Wratsch* 1910, p. 461.

Burow, *Münchener medizinische Wochenschrift* 1910, No. 34.



of animals treated with guaiacol-arsenic also showed bactericidal properties. Animals previously treated with guaiacol-arsenic remained healthy after infection with tubercle bacilli, while those not previously treated died in about 4 weeks. From these results the author concludes that guaiacol-arsenic is a specific remedy for tuberculosis.

Special interest has of late been awakened in a guaiacol preparation intended for the treatment of tuberculosis, -viz., guaiacose. This is a fluid somatose containing about 7 p. c. of calcium sulphoguaiacolate. This remedy has an agreeable taste. Three tablespoonfuls are given daily for 4 to 6 weeks. L. Haagner gives guaiacose as a rule shortly before meals, which enables its effect of increasing the appetite to come into play. If there are any signs that it is not agreeing with the patient, it is prescribed after food. Haagner found the favourable action to commence after 8 days; after 14 days there is usually some gain in weight, while after 4 to 6 weeks there is, as a rule, a striking improvement in the general condition and in the objective symptoms. The expectoration is greatly improved, and the purulent sputum assumes a better appearance. The author obtained the best results in apical catarrh and in commencing pulmonary tuberculosis.

Pure guaiacol has been tried by N. Maldarescu in a systematic way in leprosy. No definite cure was obtained by the internal or external use of the remedy in any case, but old chronic ulcers were made to cicatrize by its use. The author directs that 1 gramme (15 grains) of guaiacol be given in the form of pills every day for 14 days. An interval of 5 days is then allowed, when a further course of pills is given for 14 days. Externally guaiacol was applied in solution to the infiltrated and ulcerated parts of the skin, and the patient was given a soda bath twice a week. The treatment caused the ulcers to heal, and also produced a distinct improvement in the general condition, with a gain in weight.

The use of iodo-guaiacol\*) is mentioned by L. Cocco. He

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Haagner, Wiener medizinische Zeitung 1910, No. 29.

Maldarescu, Spitalul 1910, No. 6.

\*) See Merck's Reports 1907, p. 143.

Cocco, Gazzetta degli ospedali e delle cliniche 1910, No. 34.

— Wiener klinische Wochenschrift 1910, No. 31.

prescribed it in the manner already described, as a 1 p. c. solution in equal parts of alcohol and glycerin. This is injected intramuscularly in quantities of 5 to 20 c. c. (85 to 340 min.). In cases of surgical tuberculosis this treatment is said to have been of good service. In suppurating lymphatic glands the solution was also injected locally after the removal of the pus. Finally, good results were obtained by painting with the solution in pharyngitis, tonsillitis and stomatitis. G. Ciuffi gave injections once a day, or once every other day, of 1 c. c. (17 min.) of a solution of 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains) of iodo-guaiacol in 10 c. c. ( $\frac{1}{3}$  oz) of oleum amygdalæ dulcis, though he did not neglect local and surgical treatment. His results were satisfactory in sclerodermia, scrofulous skin affections, lupus and lymphoma.

### Gynoval.

The unanimous opinions of Silbermann, G. Flatau, F. Nitsche, W. Siebold and Raschkow show gynoval\*) to be a useful preparation of valerian which gives results as good as those obtained with other compounds of this drug, while it is distinguished by causing little or no trouble to the stomach. Silbermann mentions palpitation and conditions of fear as the chief indications for the preparation. In these cases it almost invariably gives good results. Particularly fear at night is greatly benefited by taking two gynoval perles, and quiet sleep is obtained. In cases of frequent pulse of nervous origin it also gives good results, although in such cases the action is not always immediate and it may not show itself until repeated doses have been taken. Occasionally after taking gynoval troublesome eructation is noticed. Raschkow therefore tried gynoval perles in gelodurate capsules. These are not dissolved and absorbed until they reach the intestines. With this method of administration no eructation is set up. Silbermann believes, however, that gynoval in gelodurate capsules suffers a retar-

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Ciuffi, Gazzetta degli ospedali e delle cliniche 1910, No. 27.

Silbermann, Therapeutische Rundschau 1910, No. 15.

Flatau, Therapie der Gegenwart 1910, No. 7.

Nitsche, Klinisch-therapeutische Wochenschrift 1910, No. 36.

Siebold, Allgemeine medizinische Zentralzeitung 1910, No. 28.

Raschkow, Therapeutische Monatshefte 1910, No. 5.

\*) See Merck's Reports 1909.

dation in its action, and this is particularly to be avoided in the symptomatic use of valerian. Flatau reports on 20 cases of nervous conditions with palpitation, fear and cardiac pain with insomnia, in which gynoal gave good results. The good effect of the remedy in a case of habitual vomiting during railway journeys was remarkable.

Nitsche, Siebold and Raschkow were very well satisfied with the action of gynoal in almost every case of nervous insomnia, nervous headache, neurasthenia, severe palpitation, hysterics, intercostal neuralgia, neuralgic pain, hysterical cardialgia, epilepsy, giddiness, arterio-sclerosis and traumatic neurosis. Patients who suffer from eructation after the use of the remedy are advised to take a hot drink shortly after taking the perles, for in Raschkow's experience this tends to remove the taste of valerian.

As a rule 3 to 4 gynoal perles a day are enough, but if the action is not sufficient as many as 6 perles may be given.

### Hectin.

F. Balzer has contributed another paper\*) on the value and the method of using hectin in the treatment of syphilis. He states that before using hectin or any other arsenic or mercury treatment patients should be examined, particularly as to the condition of the optic nerves. If the patient has at any time suffered from optic neuritis, retinitis, choroido-retinitis, etc., it is best not to use arsenic treatment. If there is any doubt as to whether we are dealing with congenital syphilis, tabes, Bright's disease, etc., or whether the acuity of vision is different in the two eyes, a careful examination of the eyes should be made. If any eye symptoms show themselves during the treatment, the further use of the remedy must be left off at once, and a further examination made. With regard to the dosage of hectin, the amount to be given daily is from 0.02 to 0.04 gramme ( $\frac{1}{3}$ — $\frac{2}{3}$  grain) of arsenic, that is to say 0.1—0.2 gramme ( $1\frac{1}{2}$ —3 grains) of hectin. These doses are not excessive, for hectin is very rapidly eliminated, and thus has no cumulative action. Four or five days after the close of the

Balzer, Presse médicale 1910, No. 31, p. 274.

\*) See Merck's Reports 1909.



treatment no more arsenic is said to be found in the urine. It is advisable with hectin, as with other arsenic preparations, e. g., the cacodylates, not to give the remedy for a long time without interruption. Balzer as a rule allows an interval of 4 to 5 days after 10 injections. The author gives the following further directions: During the first week of treatment 0.1 gramme ( $1\frac{1}{2}$  grains) of hectin in 1 c. c. (17 min.) of water is injected into the muscles every other day. An equal dose is then given every day until altogether 2 to 3 grammes (30—45 grains) have been given for a complete course of treatment. The result is better if 0.1 gramme ( $1\frac{1}{2}$  grains) is given during the first 4 to 5 days, and then 0.2 gramme (3 grains) every other day, until the above total quantity has been administered. This forced treatment is particularly advisable in malignant syphilis, and in severe syphilitic symptoms. As a rule, however, doses of 0.05 to 0.1 gramme ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains) a day are sufficient to effect a cure. We must not forget that hectin, like the cacodylates and the methyl-arsenates, not only possesses a specific action, but also has a tonic effect. In infants doses of 0.02 gramme ( $\frac{1}{3}$  grain) are given, and if these are well tolerated, doses of 0.05 gramme ( $\frac{3}{4}$  grain). In children doses of 0.05 to 0.1 gramme ( $\frac{3}{4}$ — $1\frac{1}{2}$  grains) are used. Of course the back of the eye must first be carefully examined. Hectin may also be given by mouth, only its action is less pronounced with the same doses.

“Hectargyre” is the name given by Balzer to a solution of 0.1 gramme ( $1\frac{1}{2}$  grains) of hectin and 0.01 gramme ( $\frac{1}{6}$  grain) of mercuric oxycyanide in 1 c. c. (17 min.) of water. This dose is injected once a day. The treatment is usually continued for 20 days until a total of 2 grammes (30 grains) of hectin has been used, but the treatment may be extended to 30 days if necessary. In syphilitic nephritis a reduction of the daily dose to 0.5 c. c. (8 min.) is advised. In secondary syphilis the author obtained very satisfactory results with the use of this preparation. In most cases one or two courses of treatment are sufficient to cause the subsidence of the symptoms, and to carry the illness into a latent stage.

H. Hallopeau hopes to obtain very favourable results with the “abortive” treatment of syphilis by means of

hectin. The treatment consists in injecting the preparation locally, i. e., subcutaneously under the chancre along the lymphatic vessels in the penis. For this purpose 0.1 gramme ( $1\frac{1}{2}$  grains) of hectin in 2 c. c. (34 min.) of water are required for a dose, given once a day. The patients are at the same time treated in the usual manner with mercury and potassium iodide. The treatment takes 30 days, and is said to give better results than intragluteal treatment with hectin.

### Hedonal.

Hedonal has of late years been recommended as an aid to ether and chloroform anæsthesia. Recently it has been found to be applicable by itself as an anæsthetic for operations, especially if it be applied intravenously. S. P. Fedoroff proved, by animal experiments, that intravenous injections of the remedy are free from danger, and are well tolerated. In man he gave it per rectum (in his first report), and intravenously, the patients being given 3 to 4 grammes (45—60 grains) of hedonal in mucilage per rectum 2 hours before the operation, and a 0.75 p. c. of hedonal solution intravenously immediately before the operation. Anæsthesia was usually obtained after the infusion of 2 to 300 c. c. ( $6\frac{2}{3}$ —10 oz) of this solution, and could be maintained by 50 to 100 c. c. ( $1\frac{3}{4}$ — $3\frac{1}{3}$  oz), so that in all about 6 to 10 grammes (90—150 grains) of hedonal were used for a single anæsthesia. In a further communication the author states that he simplified the procedure, for he had found that the rectal use of the remedy could be omitted without disadvantage. He now gives the following directions: Shortly before the operation a curved needle is inserted into the peripheral part of the vein, and a filtered 0.75 p. c. solution of hedonal in normal saline solution, warmed to 40 to 41° C., is injected. After 100 to 150 c. c. ( $3\frac{1}{3}$ —5 oz) of this solution have been infused the patient becomes drowsy, and 2 to 3 minutes later, after about 300 c. c. (10 oz) have been used, deep sleep sets in. The corneal reflexes are not abolished at first, though after 200 to 300 c. c. ( $6\frac{2}{3}$ —10 oz) more have been used anæsthesia is usually complete. In weak,

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Fedoroff, Zentralblatt für Chirurgie 1910, No. 9. — Russisches Journal für Geburtshilfe und Gynäkologie 1910, No. 5 and 6.

debilitated persons this may be the case after the exhibition of 250 c. c. ( $8\frac{1}{3}$  oz), in other cases it may be that 1000 c. c. ( $33\frac{1}{3}$  oz) are required to produce anæsthesia. With regard to the rate of flow of the infusion, this is not immaterial, for if injected too quickly breathing stops and slight cyanosis may occur. In Fedoroff's experience the optimum of quantity and flow of infusion is reached when 100 c. c. ( $3\frac{1}{3}$  oz) are injected in one minute. The quantity of hedonal solution required for an operation varied in the author's account between 400 and 1800 c. c. ( $13\frac{1}{3}$ —60 oz). When correctly applied the anæsthesia thus obtained is accompanied by practically no disadvantages. Headache, nausea or vomiting were never observed except after very complicated laparotomies, when vomiting occurred in a few cases. The operations described by Fedoroff show that under hedonal anæsthesia the most severe and painful operations may be undertaken, e. g., the resection of the Gasserian ganglion, and of the gall bladder. Special importance may attach to hedonal anæsthesia in operations on the head and neck, for by dispensing with an inhalation mask the part of the body under treatment is more readily accessible. Kidney disease forms no contra-indication to its use.

A. T. Sidorenko also obtained satisfactory results with intravenous hedonal anæsthesia. He states that to prevent disturbance of respiration 50 to 60 c. c. ( $1\frac{3}{4}$ —2 oz) must be allowed to flow in a minute. After the operation excitation may set in, or the tongue may fall back, so that the patient must be carefully watched.

Krawkoff, who has used chloroform-hedonal anæsthesia for years, attributes to it the following advantages: The stage of excitation is considerably shortened or abolished, the anæsthesia runs a uniform course, and even with the prolonged use of chloroform no cardiac or respiratory symptoms occur. By the previous administration of large doses of hedonal (about 3 grammes [45 grains]) the amount of chloroform required is reduced, and the symptoms after the anæsthesia has passed off are much milder, or remain absent\*).

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Sidorenko, Zentralblatt für Chirurgie 1910, No. 37.

Krawkoff, Russkij Wratsch 1910, Therapeutische Monatshefte 1910, p. 444.

\*) See Merck's Reports 1906, p. 124.



### Hegonon.

Hegonon is a silver nitrate ammonia albumose obtained by the action of silver nitrate ammonia on albumoses. It contains about 7 p. c. of silver, there is no free ammonia present and it is soluble in water in the proportion of 1:10. The alkaline reaction of the dilute solution is due to the alkalinity of the silver nitrate ammonia. A special advantage of the preparation, which makes it very well suited for the treatment of gonorrhœa, lies in the fact that it does not cause the coagulation of albumoses either in a cold or warm solution. The first trials with this new remedy for gonorrhœa were carried out by Klingmüller. He used it in a 0.25 p. c. aqueous solution, of which an injection was given 4 to 6 times a day. In addition to the injections the urethra was occasionally washed out with solutions of 1:6000 to 1:2000. The results thus obtained were very satisfactory. 38 patients were treated, and were cured on an average in 22 days.

To prepare a hegonon solution the preparation is gradually strewn on to water at the ordinary temperature, and the water is stirred with a glass rod for 1 to 2 minutes. In another 1 to 2 minutes it has dissolved. The solution must be kept in well stoppered bottles of amber tinted glass.

### Hirudin.

In connection with previous accounts in these Reports, the publications of A. Dienst are important. He attributes eclampsia gravidarum to a flooding of the blood with fibrin, and he therefore favours the use of hirudin. F. Engelmann, whose results with hirudin have been already recorded in these Reports\*), points out that F. Volhard made the suggestion that the action of fibrin ferment in eclampsia might be abolished by means of extract of leech. Volhard also expressed his misgivings

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Klingmüller, Münchener medizinische Wochenschrift 1910, No. 32, p. 1680.

Dienst, Archiv für Gynäkologie 1908, No. 2. — Zentralblatt für Gynäkologie 1909, No. 50.

Engelmann, Zentralblatt für Gynäkologie 1910, No. 5.

\*) See Merck's Reports 1909, p. 230.

Volhard, Monatsschrift für Geburtshilfe und Gynäkologie 1897, No. 5.

with regard to its use. He considers the remedy to be dangerous, especially in cases in which its action is most prominent, for by abolishing the coagulability of the blood we introduce the danger of post-partum hæmorrhage. Engelmänn's experience extends to 6 cases of eclampsia. He utters a warning against undue optimism regarding hirudin treatment. We are not yet in a position to abolish the bad effects of eclampsia, we are merely able to suppress its advance. In his opinion the chief aim should therefore be early delivery, while hirudin treatment takes a place of secondary importance. In severe cases, however, the dose of 0.2 to 0.3 gramme of hirudin, already suggested (see Merck's Reports 1909, p. 230) is too low. The remedy is by no means without action, as 1 gramme is sufficient to render the blood fluid for 3 to 4 hours, consequently rather larger doses than 0.3 gramme are required. This may be risked, for these doses are well tolerated. If the convulsions recur the hirudin treatment may be repeated after 3 hours.

The toxicity of hirudin is illustrated in a paper by W. Sievert, who made experiments with hirudin in animals, and came to the following conclusions: Hirudin has toxic properties; if given to a rabbit intravenously in doses of 0.1 gramme it causes increased frequency of respiration, a rise of temperature, apathy and somnolence, and also albuminuria. Rasch says repeated hirudin injections may have a fatal action. The author also pointed out that hirudin solutions when warmed to 60—100° C. partly lose their toxic properties. Finally Sievert dealt with the question of activating mercury by hirudin as described and investigated by M. Kohan, Prussak and Priebatsch. He was able to confirm the increase of the toxic action of mercury produced by hirudin, but at the same time he found that hirudin itself had a poisonous action. He therefore suggests the possibility that the increased toxicity of mercury following the use of hirudin is due to the combined toxic action of the two substances.

Sievert, *Zeitschrift für experimentelle Pathologie und Therapie* 1909, Vol. VII, No. 2, p. 532.

Kohan, *Archiv für experimentelle Pathologie und Pharmakologie* Vol. 61, p. 132.

Prussak, *Archiv für experimentelle Pathologie und Pharmakologie*, Vol. 62, p. 201.

Priebatsch, *Virchows Archiv*.

**Hordenine sulphate.**

A Martinet has written a paper on the value of this preparation\*) in intestinal affections. He found it to possess very slight toxic properties, for the lethal dose on intravenous application in dogs and rabbits is 0.25 gramme per kilogramme of body weight. In adults he found that subcutaneous doses of 0.75 gramme (11 grains) might be given daily, and internally as much as 3 grammes (45 grains) without fear of producing marked disturbance. In dysentery it may be given in still larger doses. In adults it should be given for considerable periods in doses of 4 to 6 grammes (60—90 grains) a day, and in children in doses of 1 to 2 grammes (15—30 grains) daily, and it does no harm. In addition to its action in tropical dysentery, hordenine possesses the power of paralyzing peristalsis similar to that of opium or morphine in acute diarrhœa due to unsuitable feeding, and in muco-membranous enteritis. It is far less toxic, however, than these drugs. In children the action of the remedy is not so marked as in adults. Martinet therefore considers that it has no advantage over the ordinary methods of treating diarrhœa in children. In adults, however, it is well worth trying in typhoid fever with profuse diarrhœa.

**Hydrargyri benzoas.**

Last year I reported on the use of mercuric benzoate in syphilis as suggested by Hallopeau, and pointed out that the pain produced by a solution of mercuric benzoate may be relieved by the addition of sugar (saccharose). The suggestion to use sugar as an anæsthetic is due to Fleig, and has been tested and modified since by Desmoulière and Lafay. Fleig found that sugar was a very suitable means of preparing isotonic and hypertonic artificial sera, and that it could be injected without harm in a concentration as high as 30 p. c. Saccharose was so well tolerated that Desmoulière and Lafay were led to add saccharose to the normal saline solution used for the injections. Having confirmed the fact that this procedure is harmless, they used the following solution:

\*) See Merck's Reports 1909.

Martinet, *Presse médicale* 1910, No. 73, p. 683.

Fleig-Desmoulière-Lafay, *Répertoire de pharmacie* 1910, No. 10, p. 453.



Rp. Hydrarg. benz.	1.0 gramme (15 grains)
Sod. chlor.	1.0 gramme (15 grains)
Sacchar.	10.0 grammes ( $\frac{1}{3}$ oz)
Aq. destill.	ad 100 c. c. ( $3\frac{1}{3}$ oz)

The saccharose may be replaced by glucose or milk sugar, but the authors prefer the former as it may be obtained in greater purity. In the treatment of diabetes, however, milk sugar has an advantage, for in this case saccharose causes unpleasant effects. The results obtained with sugar are said to be so good that when injecting soluble salts of mercury the use of cocaine may be dispensed with, and as a rule it cannot be used in any case, for it forms with mercury salts double salts that are sparingly soluble. Mercury and iodine is also contained in the following solution for injection:

Rp. Hydrarg. ioidid. rubr.	1.0 gramme (15 grains)
Sod. ioidid.	1.0 gramme (15 grains)
Sacchar.	10.0 grammes ( $\frac{1}{3}$ oz)
Aq. destill.	ad 100 c. c. ( $3\frac{1}{3}$ oz)

These solutions have, however, one disadvantage. They do not stand thorough sterilisation, for sugar tends to reduce the mercury salts when heated. The authors therefore suggest filtering the solutions through porcelain candles.

### Hydrargyri iodium rubrum.

A few years ago much trouble was taken in the preparation of mercuric oxide ointment of very fine grain for ophthalmic practice\*). Von Ammon has now given directions for the preparation of eye ointments containing very finely divided mercuric iodide and mercurous iodide (Hydrarg. ioidid. rubr. and hydrarg. ioidid.). The following method is given of preparing unguentum hydrargyri biniodidi: A solution of 1.5 grammes of potassium iodide in 400 c. c. of water is poured into a solution of 1.2 grammes of mercuric chloride in 300 c. c. of water at 50° C. The supernatant liquid is poured off, and the precipitate is washed with water until the washings are free from chlorine. The precipitate consists of 2 grammes of biniodide of mercury.

\*) See Merck's Reports 1904, p. 95.

v. Ammon, Münchener medizinische Wochenschrift 1910, No. 9, p. 473.

It is placed in a tared capsule with the necessary quantity of water, and is allowed to settle thoroughly, the water is then poured off until only 5.5 grammes remain. The residue is worked into an ointment with 14.5 grammes of anhydrous lanoline. In this way 20 grammes of a 10 p. c. mercuric iodide ointment are obtained. An ointment of the required dilution is prepared from this concentrated ointment; usually a 0.5 or 1 p. c. ointment is used. Similarly an unguentum hydrargyri iodidi pultiforme may be prepared from mercurous nitrate, due regard being had to its properties.

These ointments contain the active salt of mercury in exceedingly fine subdivision, and give a guarantee of immunity from irritant action on the tender tissues of the eye, and further that the active salt is thoroughly used up.

Unguentum hydrargyri iodidi pultiforme 1 p. c. is used by the author in the treatment of phlyctenulous eye troubles, especially in the so-called marginal phlyctenules. With a suitable dressing the ointment leads to a cure of all signs of the disease. The same effect is obtained in corneal phlyctenules and their sequelæ, in which the absence of inflammation points to a lack of tendency to heal. The ointment was also found useful in blepharospasm due to rhagades at the outer canthus of the eyelid, and in all scrofulous affections of the eyes and diseases of the margins of the lids.

Unguentum hydrargyri biniodidi pultiforme (0.3 to 0.5 p. c.) is used by the author in chronic blepharitis coupled with considerable desquamation. If the ointment is left too long in the conjunctival sac it produces inflammation. Ammon consequently found it advisable to increase the strength of the ointment gradually from 0.3 p. c. to 0.5 p. c. while carefully observing the effect, and to place the ointment on the margin of the closed lids. By repeatedly stroking with a glass rod the remedy is made to penetrate into the ciliary bodies. After acting for 3 to 5 minutes the ointment is wiped away, and the scales are removed by means of a moist pledget of gauze. This treatment may be repeated once or several times at a sitting, according to the degree of the disease. If inflammation commences, or thick crusts form, the margins of the lids are softened by preliminary treatment with biniodide of mercury ointment applied the

previous night by means of a suitable dressing. The treatment must be repeated every 4 to 12 days, according to the degree of chronicity of the trouble, and occasionally requires to be continued for months. It gives satisfactory results even after other remedies have been used for years without success.

### **Hydrargyrum metallicum.**

For many years attempts have been made to use mercury in the form of all manner of inorganic and organic compounds in the treatment of syphilis; E. Richter, however, has returned to the use of metallic mercury. So far he has used it subcutaneously, and has shown that metallic mercury is far less dangerous than we could have expected from our knowledge of its use in the form of ointments or of the volatilized metal. He proved this fact by giving a rabbit an intravenous injection amounting to 1 p.c. of its weight of mercury (1 c.c. = 13.56 grammes) without any visible effect on its appetite, its power of movement and its condition in general. In man he has injected as much as 6 grammes at a time into the fatty tissue of the nates. He selected this spot because here the metal disappears without leaving thickening and without causing pain.

In syphilis the author has so far treated 25 patients with injections of mercury. To judge by his account the treatment possesses great advantages. Mercury shows no toxic action, and in the doses required (0.5 to 1 c.c. in all), no secondary mercurial symptoms, such as mercurialism or stomatitis, are produced. Neither has the author found albumin or sugar in the urine in his cases. He suggests the following experiments to decide whether the primary disease is prevented from causing its late effects. In the case of a syphilitic patient with a primary lesion, a thin thread or drop of quicksilver should be injected under the skin of the penis in all the lymphatic regions which carry the syphilitic virus from the primary lesion. The author believes that it will be possible in this way to determine whether secondary and tertiary syphilis may be suppressed by

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Richter, Berliner klinische Wochenschrift 1910, No. 34, p. 1588.

Richter, Archiv für Laryngologie und Rhinologie, Vol. 23, No. 3.

— Münchener medizinische Wochenschrift 1910, No. 44, p. 2317.



mercurial treatment, or even prevented entirely. In any case the new method is worth investigating.

In another publication on the injection of mercury in syphilis of the throat and nose, E. Richter states that he used doses not exceeding 0.1 to 0.2 gramme, so as to avoid stomatitis and gingivitis. He gave 3 to 4 injections within 5 days. At the same time as the mercury he applies an aqueous solution of quinine hydrochloride or soda solution to prevent air entering the syringe, and to enable the mercury to reach the organism more readily.

### **Hydrargyri nitras.**

Some time ago J. Jefimow recommended liquor Bellosti as a reagent for helminthiasis. He had found that the urine of patients suffering from worms contained a substance which produced a black or grey precipitate when this reagent was added to the boiling urine, while in normal urine a white precipitate is obtained on the addition of the mercury solution. The reaction obtained by Jefimow is not quite reliable, as is clear from a communication by A. Butenko. In his experience the urine of paralytic patients gives a grey or black precipitate with liquor Bellosti in about 90 p.c. of the cases, even when the patients are entirely free from helminths. The reaction does not depend on the physical condition of the urine of paralytic subjects, nor is it due to the presence of indican or similar substances which give Ehrlich's reaction with dimethyl-amidobenzaldehyde, or the diazo-reaction. It may be taken as fairly certain, however, that it is due to pathological substances produced by the paralysis, for the author was able, at any rate in a few cases which tended to improve, to show that the reaction disappeared from the urine. In by far the greater number of cases, however, the reaction shows no tendency to disappear after it has once appeared. In cases in which the reaction does disappear it shows that the disease is subsiding, and is therefore of prognostic value. Again, if the reaction becomes very intense, we have a sign that the disease is advancing. As a diagnostic aid Butenko found the reaction

Jefimow, Merck's Reports 1907, p. 127. — Zentralblatt für Kinderheilkunde 1907, No. 5, p. 152.

Butenko, Russkij Wratsch 1910, No. 2. — L'Italia sanitaria 1910, No. 15, p. 303. — Rivista critica di clinica medica, Vol. 11, 31.

of great service, for (apart from helminthiasis) this reaction is not obtained in dementia præcox, in alcoholic psychoses, periodic psychoses, cerebral arterio-sclerosis, epilepsy or dementia senilis.

Liquor Bellosti is best prepared fresh by dissolving 1 gramme of mercurous nitrate in crystals in 8 grammes of water and 2 grammes of nitric acid (25 p.c.). If it is to be kept for some time, a little metallic mercury must be added.

### **Hydrargyri oxycyanidum.**

Contributions to the treatment of syphilis with oxycyanide of mercury have been made by Jessner and Eckermann. Jessner used the preparation in place of corrosive sublimate with satisfactory results. He uses a combination of oxycyanide of mercury and alypin in preference to Hirsch's injections. He injected 1 c.c. daily of a 1 p.c. solution of the mercury salt, of the 2 p.c. solution 1 c.c. 3 times a week. No anæsthetic is required as a rule, but if it be desired to use one alypin nitrate is the best, for it forms no precipitate with the oxycyanide in an aqueous solution. The author usually prescribes:

Hydrarg. oxycyanid.	0.3—0.6	gramme (5—10 grains)
(Alypin. nitr.	0.15	gramme) ( $2\frac{1}{3}$ grains)
Aq. destill.	30.0	grammes (1 oz)

There would be no danger in injecting still stronger solutions at longer intervals, for the oxycyanide produces very slight irritant effects. The author never observed a hard, infiltrated patch, and as a rule by the time the next injection was given there was no sign of the previous one.

This treatment led to the rapid subsidence of the secondary appearances, the general condition, frequently much affected by syphilitic toxins, improved in a short time. In a word, the action was always a prompt one. The secondary effects never lead to permanent injury, provided the patient is carefully watched. Eckermann considers the combination of oxycyanide of mercury and alypin nitrate suggested by Jessner to be less painful than the combination of the oxycyanide with acoin.

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Jessner, *Therapeutische Monatshefte* 1910, No. 2.

Eckermann, *Fortschritte der Medizin* 1910, No. 3.

A. Strauss reports on a case of secondary ulcerous syphilis in which the use of salvarsan had been followed by a change for the worse, which was very rapidly put right by treatment with oxycyanide of mercury. After 3 injections of a 1 p. c. solution of oxycyanide of mercury the ulcers had become clean, and the necrosed tissue was almost completely thrown off. The external application of calomel powder then led to a very satisfactory advance towards a cure.

### **Hydrargyri salicylas.**

Dreuw found it no uncommon occurrence for emulsions of salicylate of mercury with olive oil or liquid paraffin to clog the needle of the Pravaz syringe. He therefore recommends in such cases to place the needle with the cannula inverted into the glass cylinder of the syringe filled with the mass for injection, and by pressure on the piston rod to express the particles which are clogging the needle. A still simpler suggestion is given by Porges to prevent clogging of the needle from the first. Porges found that however carefully the emulsion of salicylate of mercury might be prepared, the salicylate of mercury would separate out on standing, and form a more or less viscid layer which adheres somewhat firmly to the bottom of the glass vessel. By shaking or stirring it is not possible as a rule to loosen this layer uniformly, and there is danger that too little mercury may be contained in the quantity injected, or that the cannula may become clogged. This may be readily prevented by placing in the bottle containing the emulsion some so-called porcelain or glass shot (little marbles of about 3 mm. diameter) which have been well cleansed before use with hydrochloric acid and water and then dried. If the bottle is now shaken, nothing adheres to the glass, and no particles are formed of sufficient size to clog the cannula. Further, the drug is uniformly mixed with the oil, so that each syringeful contains the right quantity of mercurial salt.

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Strauss, *Medizinische Klinik* 1910, No. 49.

Dreuw, *Monatshefte für praktische Dermatologie* 1910, Vol. 51, No. 8, p. 348.

Porges, *Monatshefte für praktische Dermatologie* 1910, Vol. 51, No. 12, p. 562.



In this way the emulsion may be used even after it has stood for months.

### Hydropyrine.

Hydropyrine, the sodium salt of acetyl-salicylic acid\*) has been reported on by A. Fickler. As an antipyretic it causes a fall of temperature, which is very often accompanied by fairly severe sweating. The fall amounts to 1·5 to 2° C. with a dose of 0·5 gramme ( $7\frac{1}{2}$  grains), and to 2 to 3° C. with a dose of 1 gramme (15 grains). In articular rheumatism the preparation is said to display the same specific action as sodium salicylate. The author gave it for 3 days in doses of 0·5 gramme ( $7\frac{1}{2}$  grains) every 2 hours, with the result that the attack was cut short, and the joint swellings rapidly subsided. In arthritis deformans the symptoms were much relieved with doses of 0·5 gramme ( $7\frac{1}{2}$  grains) of hydropyrine. With regard to the antineuralgic and analgesic action of the remedy the results were variable in neuralgia, practically absent in a case of visceral neuralgia, satisfactory in intercostal neuralgia and cephalalgia, and good in itching due to urticaria. It was also of good service, in combination with dionin, (0·1 dionin, 5·0 hydropyrine in 150 water: 1 tablespoonful 3 times a day) in dysmenorrhœa. To excite diaphoresis 2 doses of hydropyrine, of 1 gramme (15 grains) each, are given with an interval of an hour between each dose, and the patient may be swathed in woollen cloths to enhance the effect. The diuretic properties of hydropyrine were shown in pleurisy with effusion, in which the desired result was obtained by giving 0·5 gramme ( $7\frac{1}{2}$  grains) 3 times a day.

### Ichthyol.

From a communication on the cause and treatment of ecthyma and lymphangitis by R. Lutembacher the following remarkable method of treatment is taken:

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\*) See Merck's Reports 1908.

Fickler, Deutsche medizinische Wochenschrift 1910, No. 48, p. 2248.

In a later paper the author points out that Hydropyrine is the name now applied to the lithium compound of acetyl-salicylic acid, the sodium salt being too unstable.

Lutembacher, Revue internationale de médecine 1910, p. 22. — Allgemeine medizinische Zentralzeitung 1910, p. 308.

The local treatment consists in the use of compresses soaked in 5 p.c. solution of ichthyol, and later in a 10 p.c. solution. The whole of the inflamed zone and of the lymphangitic strands are packed with compresses soaked in this solution. The affected part is then covered with a layer of wool, over this a layer of waxed paper is placed and the whole is fixed with a linen or gauze bandage. The dressing must be changed every day. Under its influence the inflammatory and lymphangitic process subsides, and the pustules dry up. As soon as the diffuse inflammation has disappeared, leaving only the ecthymatous ulceration, a 10 p.c. ichthyol solution is used for the dressings, while the whole region of skin surrounding the ulcerated area is treated with zinc ointment. Care must be taken that no new pustules appear, and when this is the case they must be destroyed by the thermo-cautery or the point of a scarifier. The patients frequently re-infect themselves over and over again by scratching the efflorescences. The dressings must therefore be changed under the doctor's supervision. As soon as the ulcers are clean an attempt is made to get them to cicatrize by suitable powders (dermatol, ectogan). In addition to this treatment the general treatment must not be neglected. This is especially necessary in cases in which in addition to ecthyma there are furuncles, folliculitis and pyodermatitis. The author therefore recommends enemata, purgatives and a milk diet.

Ichthyol also appears to be specially valuable, to judge by F. Bruch's accounts, in the treatment of furuncles in the external auditory meatus if the patient objects to an incision, or if an incision has been made, to carry on the treatment. For this purpose a mixture of equal parts of ichthyol and glycerin is placed in the auditory meatus by means of a pledget of wool. The meatus is closed with a tampon of wool to prevent the ichthyol from escaping or drying up too quickly. If the external auditory meatus is permeable, which is necessary for the success of the treatment, the sedative action of ichthyol is very soon apparent. The ichthyol tampons are inserted once a day, in specially painful cases twice a day. With this treatment the plug of wool is frequently found soaked with pus the

next day, the ichthyol having caused the furuncle to open and thus allow the pus to escape. The auditory meatus is covered with a disinfectant layer of ichthyol, so that it is protected from the spread of the furuncle. Relapses are also prevented by this means, so that the application of ichthyol is indicated even after incision. It should be continued until the furuncle has dried up completely.

### Indian ink (Burri).

A simple method of obtaining pure cultures of bacteria, under microscopical control from the time of proceeding from each individual cell, has been described by R. Burri. For this purpose he used a specially prepared Indian ink, which may also be used with advantage in place of various stains, as, for instance, in the demonstration of spirochætæ. It is prepared from fluid commercial Indian ink by diluting with 10 parts of water, and then sterilising this dilution. Burri's method of demonstrating the spirochæta pallida is based on the following fact: If Indian ink is added to the material under investigation, and is spread in as thin a layer as possible, there is seen under the microscope an almost homogeneous or dark-brown coloration of the ground, for the exceedingly small grains of Indian ink lie close together. If formed elements are present in the film, no grains of Indian ink are able to adhere to these parts. Hence, transparent bodies like bacteria are easily recognised as transparent structures. The field of view thus resembles to some extent a photographic negative. W. Scholtz found the Indian ink method successful in the case of material in which spirochætæ were present in considerable numbers, provided the original material did not contain too much pus. He directs that the Indian ink preparations should be made as follows: A small drop of serum from the material under investigation, containing a little blood, is placed on a slide. It is well mixed with a drop of distilled water of about the same size; of this mixture a small drop is mixed on a slide with about half its quantity of liquid Indian ink. This is spread upon the slide by means of a platinum loop after breathing upon the glass, and is allowed to dry. A suffi-

Burri, Zentralblatt für Bakteriologie 1907, Vol. 20, II., p. 95. — Burri, Das Tuscheverfahren, Jena 1909.

Scholtz, Deutsche medizinische Wochenschrift 1910, No. 5.



ciently clear preparation may also be obtained, according to J. Berg, by using a more fluid Indian ink instead of diluting it with water. Petersen has obtained very satisfactory results with Burri's method, and considers it well suited for consulting room examinations, because it can be carried out rapidly.

### **Iodine.**

About 2 years ago Grossich recommended a method of disinfecting the skin before operations which aroused considerable interest among surgeons. The method consists in painting the field of the operation with tincture of iodine (10 p.c. iodine). It is not necessary to clean the skin beforehand, and washing with soap is to be avoided. After the operation the margins of the wound are painted with tincture of iodine to obtain the best possible healing. This method was found by Unger very valuable in urgent cases, for the patient could be prepared for operation within 2 minutes, and in cases with copious suppuration in the abdominal cavity and the extremities, in which prolonged washing might be dangerous on account of the shock accompanying this procedure. Not only is the method very simple, and an important point is the fact that it is certain in its action, but it fulfils all practical requirements. This is confirmed among others by R. Brewitt, E. W. Baum, Federmann, U. Noferi, Nast-Kolb, Papinian, Ueber, Knoke, Berard and Chattot, Streitberger,

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Berg, Deutsche medizinische Wochenschrift 1910, No. 20.

Petersen, Russkij Wratsch 1910, No. 32.

Grossich, Zentralblatt für Chirurgie 1908, p. 1285 (see also 1910, No. 21).

Unger, Berliner klinische Wochenschrift 1910, No. 2.

Brewitt, Münchener medizinische Wochenschrift 1910, No. 6.

Baum, Medizinische Klinik 1910, No. 12.

Federmann, Berliner klinische Wochenschrift 1910, No. 7.

Noferi, Riforma medica 1910, No. 6.

Nast-Kolb, Münchener medizinische Wochenschrift 1910, No. 6.

Papinian, Spitalul 1909, No. 21.

Ueber, Therapie der Gegenwart 1910, No. 12.

Knoke, Münchener medizinische Wochenschrift 1910, No. 18.

Berard-Chattot, Lyon chirurgical 1910, 1<sup>st</sup> May.

Streitberger, Deutsche medizinische Wochenschrift 1910, No. 29.

M. Pap, W. Müller, Braun, Viannay, R. Bissauge, Papaioannou, Segelken and J. Grekow. In practice it has been found that painting with iodine may be used in all large and small operations, including hernia operations, a point which was in doubt at first. We now know that the only thing to avoid is contact between two contiguous surfaces of skin that have been painted with iodine. When this fact is considered, the iodine method of disinfection may be used even for the scrotum.

C. Hesse used for this method instead of the pure diluted tincture of iodine, a mixture of it with alcohol (2+8), with which he obtained equally good results. A. Bogdán modified Grossich's method by a preliminary rubbing of the patient's skin with tincture of iodine. M. Donati has also modified the method to prevent the slight disadvantages observed by a few authors. He uses a solution of one part of iodine in 100 parts of alcohol, with which the skin is rubbed 2 or 3 times. In this way it is said that the skin is never inflamed. Grossich states, further, that the inflammation of the skin produced by iodine is very slight, and that the use of undiluted iodine very seldom causes inflammation of the skin; certainly it occurs less often than is the case with the classical method of preparing the field of operation. The fear of eczema and dermatitis is exaggerated, and has undoubtedly arisen more from prejudice on theoretical grounds than from practical observation. W. Kausch also warns against the use of diluted tincture of iodine unless it is rubbed into the skin energetically for 5 minutes. He points out that tincture of iodine, if it is poured into a basin before use may become too concentrated

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- Pap, Wiener medizinische Wochenschrift 1910, No. 27.  
Müller, Deutsche medizinische Wochenschrift 1910, No. 34.  
Braun, Deutsche militärärztliche Zeitschrift 1910, No. 17.  
Viannay, Archives provinciales de chirurgie 1910, No. 2.  
Bissauge, Revue générale de médecine vétérinaire 1910, No. 178.  
— Deutsche tierärztliche Wochenschrift 1910, No. 45.  
Papaioannou, Zentralblatt für Chirurgie 1910, No. 27.  
Segelken, Klinische Monatsblätter für Augenheilkunde 1910, p. 113.  
Grekow, Archiv für klinische Chirurgie 1909, No. 4.  
Hesse, Zentralblatt für Chirurgie 1910, No. 15.  
Bogdan, Zentralblatt für Chirurgie 1910, No. 3.  
Donati, Deutsche medizinische Wochenschrift 1910, No. 13.  
Kausch, Medizinische Klinik 1910, No. 25.

by the evaporation of the alcohol, when iodine separates out, and may give rise to eczema.

K. H. Kutscher, in opposition to Grossich, advises that the application of iodine be preceded by thorough mechanical cleansing, for tincture of iodine as such possesses no appreciable bactericidal power, so that genuine sterilisation of the skin cannot be obtained by its use alone. Since soap and water cannot be used before the iodine treatment, the author believes that the skin should be cleansed with alcohol or acetone alcohol.

A comprehensive collective report on the iodine treatment of the skin before operations has been written by E. Wettstein. Those interested should refer to it.

A. Schanz, who used tincture of iodine some time ago to obtain narrow scars in operation wounds, now recommends it for the treatment of small accidental wounds such as occur in every-day life. It is said to give excellent results in such cases in place of washing with antiseptic lotions, the use of plasters and collodion. The action of tincture of iodine is said to depend on its disinfectant and slightly stimulant properties. Championnière, however, does not regard tincture of iodine as the best antiseptic, as it does not possess the anæsthetic action of phenol. He believes, further, that in very large open wounds it does not give sufficient protection against septic invasion.

Sometime ago Heussner suggested iodo-benzine. This is now reported on by Frank, G. Meyer and R. Pürckhauer. Frank considers that iodo-benzine should not be prepared from the officinal tincture of iodine, for it contains water, and is therefore not completely soluble in benzine and in liquid paraffin. It is better, therefore, to dissolve 1 gramme of iodine in 750 grammes of benzine, this takes a few hours, and then to add 250 grammes of liquid paraffin. Meyer considers a solution of 0.5 gramme of iodine in 1000

Kutscher, *Berliner klinische Wochenschrift* 1910, No. 9.

Wettstein, *Medizinische Klinik* 1910, No. 44.

Schanz, *Deutsche medizinische Wochenschrift* 1910, No. 33. —

See Merck's Reports 1908, p. 227.

Championnière, *Klinisch-therapeutische Wochenschrift* 1910, p. 668.

Heussner, Merck's Reports 1906, 1907 and 1909.

Frank, *Münchener medizinische Wochenschrift* 1910, No. 12.

Meyer, *Medizinische Klinik* 1910, No. 34.

Pürckhauer, *Münchener medizinische Wochenschrift* 1910, No. 42.



grammes of the above mixture to be sufficient. In his opinion, too, the amount of paraffin may be considerably reduced. He therefore uses a solution of 0.5 gramme of iodine in 800 grammes of benzine and 200 grammes of liquid paraffin. As an increased protection to wounds the author uses, shortly before the operation, Heussner's iodine spray which is prepared according to the following directions: 2 grammes of iodine are dissolved in 10 grammes of absolute alcohol and 10 grammes of ether; to this are added 2.5 grammes of collodion and sufficient ether to bring the weight of the mixture to 100 grammes. With this solution the entire region of the skin that has already been disinfected is thoroughly sprayed.

The disadvantages of the iodo-benzine method of disinfection include its destructive action on rubber gloves and the occasional caustic action on the skin in case the iodo-benzine should leave the portion of the body under treatment and reach parts where it is not able to evaporate. With care this mishap should be preventable. In any case it cannot affect the well-established value of the iodo-benzine method of disinfection.

O. von Herff, who considers acetone alcohol\*) to be the best known medium for cleansing the skin, recommends the use of iodine in another form after cleansing the field of operation. For the protection of wounds he uses a solution of 10 grammes of benzoin and 10 grammes of dammar in 100 grammes of ether, to which has been added 20 p.c. of a solution of 7 grammes of iodine and 5 grammes of potassium iodide in 100 grammes of alcohol.

G. Bradt has also used iodine for touching the throat and nasal cavities in whooping-cough. The author prescribes a solution of 0.5 gramme of iodine, 1.5 grammes of potassium iodide and 0.5 gramme of phenol in 15 grammes of glycerin with as much water as will bring the total weight up to 100 grammes. This solution is applied once a day, the lower part of the throat being first touched with the swab, which is then carried up to the nasal cavity as far as the roof of the pharynx, where the drug is expressed from the swab by the patient's movements. The swabbing should

Herff, *Therapie der Gegenwart* 1909, p. 573.

\*) See Merck's Reports 1909, p. 85.

Bradt, *Therapie der Gegenwart* 1910, p. 305.

not take longer than 2 to 3 seconds, as it is disagreeable to children. This treatment has a very favourable effect on the course of pertussis. It checks new cases, or cuts them short, and in every case it alleviates the disease and the attacks, at the least.

### **Iodipin.**

Comparative investigations on the elimination of iodine in inorganic and organic combination when given by mouth in man have been carried out by E. Bröking, and have led to the result that potassium iodide is by far the greater part excreted comparatively quickly during the first hours after being taken, while the compounds of iodine with fatty acids, such as iodipin, show great physiological differences with regard to their excretion when compared with the alkaline iodides. In them the elimination sets in later, and the liberation of iodine is far more uniform, and extends over a longer time, so that we are justified in stating that a depot is formed in the organism. In therapeutics these results point to important indications for the use of iodipin.

The advantages of iodipin\*) over potassium iodide are shown in a communication by O. Bondy on a case of actinomycotic parametritis. The author was obliged to give up the use of potassium iodide because of vomiting. He therefore used iodipin subcutaneously. With its use he was able to produce a slight improvement for a time. In all 100 c.c. of 25 p.c. iodipin were injected in doses of 5 c.c. daily.

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Bröking, Zeitschrift für experimentelle Pathologie und Therapie 1910, Vol. 8, No. 1.

\*) See Merck's Reports 1897—1909. — By altering the method of manufacture I am now in a position to issue iodipin in a stable form. It should be remarked that the efficacy of the new preparation is not impaired in the very least if the yellow fluid has assumed a brownish-yellow or brownish colour after long storage in the dark. If darkened iodipin is exposed to the light for a time it gradually becomes lighter in colour. When importance is attached to the use of a light yellow coloured preparation for reasons of appearance, it is recommended to remove the paper cover from the bottles and to keep them in full daylight.

Bondy, Zentralblatt für Gynäkologie 1910, No. 38, p. 1240.

In the treatment of rheumatic pain in patients known to be syphilitic, G. Daniel combined iodipin treatment with the use of salol, with good effect. He prescribed the following solution:

Rp. Iodipin (10 p. c.)      100.0 grammes ( $3\frac{1}{3}$  oz)

Phenyl. salicyl.      25.0 grammes ( $\frac{5}{6}$  oz).

The salol is dissolved with the aid of warmth in the iodipin. It crystallises out at a low temperature, and the mixture must therefore be cleared by warming before use. Daniel injected doses of 5 c. c. subcutaneously with the result that the pain quickly subsided.

The value of iodipin injections in syphilis has been mentioned by J. E. Lane. He observed cases in which the preparation gave excellent results. Buss also reports several cases of severe syphilis in which such good results were obtained with iodipin injections that the author regards it as the best known preparation of iodine. The slow absorption and elimination following its subcutaneous use keeps the patients under the influence of iodine for a longer time than is the case when iodine is given internally. Again, the stomach is not upset, and iodism very seldom occurs. The great value of iodipin in syphilis cannot be brought out more clearly than by a study of the author's cases.

### **Iodipin pro usu veterinario.**

A further contribution to the treatment of tetanus\*) with iodipin injections has been written by Frank. In horses his treatment consisted in a daily rectal application of 100 grammes of chloral hydrate in hot milk and 50 to 70 grammes of iodipin (25 p. c.), with 25 to 30 p. c. ether, which he injected subcutaneously every 1 or 2 days. The mixture was very well tolerated, apart from a short transitory excitement after the application. In one case abscesses of the skin appeared subsequently, but they healed rapidly. In the author's opinion they were caused at the seat of the puncture by rubbing against the straps, and not

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Daniel, La Clinique 1910, No. 34, p. 641.

Lane, Lancet 1910, 25th June.

Buß, Therapeutische Monatshefte 1910, No. 12, p. 676.

\*) See Merck's Reports 1909, p. 240.

Frank, Münchener tierärztliche Wochenschrift 1910, No. 13.



by the drug itself. It is a matter of common experience that the convulsions produced by the tetanus toxin are not limited to the immediate vicinity of the infected place. The poison is carried away, and becomes anchored in the nearest parts of the central organs. The author therefore tried iodipin injections on both sides of the shinbone to interrupt the poisons in their path to the neighbourhood of the nerves, blood and lymph vessels. There was at first a severe reaction, but after 48 hours, improvement set in and after 5 days the animal was out of danger. Other cases reported by Frank point to the curative value of iodipin in tetanus.

In another communication Frank describes the value of iodipin in lameness in a foal. The first foal treated by the author had shown symptoms of lameness for 2 to 3 days, which assumed the form of severe swelling of various joints. A teaspoonful of iodipin (25 p. c.) was given three times daily, and iodipin mixed with 25 p. c. of oil of turpentine was applied to the swelling. The result was surprising, for after 4 days the foal was well. In other cases iodipin was also found of great use. The author points out that especially in the case of a sucking foal the continued use of large doses may lead to acute iodipinism which quickly disappears when the internal administration of iodipin is left off, and if the treatment is left off in good time the general condition is not materially affected.

In a case of metastatic arthritis in a horse, Hentrich first washed the affected joint with Burow's mixture with the addition of camphor, and then rubbed it with a 10 p. c. ichthyol ointment. This treatment, however, only made matters worse, and the shoulder joint also became affected. This treatment was continued and the animal was now given doses of 50 grammes ( $1\frac{2}{3}$  oz) of iodipin (10 p. c.) subcutaneously in the sides of the neck, morning and evening, on two days. A successful result did not set in, however, until the author had given 50 gramme ( $1\frac{2}{3}$  oz) doses of 25 p. c. iodipin on two consecutive days. The febrile temperature rapidly came down to normal, a desire for food showed itself, movements became freer after the first in-

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Frank, *Münchener tierärztliche Wochenschrift* 1910, No. 14.

Hentrich, *Zeitschrift für Veterinärkunde* 1910, No. 7.

jection, and 3 days after the last injection there remained only slight lameness while trotting. After 4 days more the patient was well, and the joints had lost their swelling. The success of iodipin treatment was so striking in this case that there was no room for doubt. In the author's opinion iodipin undoubtedly possesses a direct antitoxic action in septic inflammation, and this has been confirmed in human medicine.

In the treatment of petechial fever J. T a n t o s has used iodipin (10 p.c.) for a number of years with very satisfactory results. In the horses to be treated he gave subcutaneous injections of 20 to 50 grammes ( $\frac{2}{3}$ — $1\frac{2}{3}$  oz) of the preparation several days in succession. As a result of the iodipin injections iodine is continuously supplied to the organism in consequence of the slow absorption of the remedy; the iodine by itself or in combination with the fatty oil contained in the iodipin displays a curative action until it has been converted into salts in the blood, and then excreted with the urine. The author's cases show that repeated or continued iodipin injections applied at the temperature of the body provide the organism with a substance that increases the opsonic index of the blood if given in good time, and enables the body to wage a successful battle with the toxins causing the petechial fever.

The value of iodipin in actinomycosis is shown by a case reported by Wucher. A calf suffering from this disease, with a tumour in the parotid region the size of a fist, was breathing heavily and exhaled a penetrating odour from the nose and throat. Two iodipin injections were given and resulted in a complete, permanent cure.

### **Iodival.**

D. S o m m e r v i l l e considers it desirable, in tertiary syphilis, to store up iodine in the neighbourhood of the syphilitic focus. This cannot be done with the alkaline iodides, for they are absorbed and excreted too rapidly. Iodival is better suited for this purpose, and the author has tried it with satisfactory results in the course of two

Tantos, Österreichische Monatsschrift für Veterinärkunde 1910, No. 2.

Wucher, Münchener tierärztliche Wochenschrift 1910, No. 21.

Sommerville, Folia Therapeutica 1909, No. 4 (October).

years in a number of syphilitic patients. The author points out above all that the preparation causes no harmful secondary effects, even after it has been given for months, to the amount of three doses of 0.3 gramme (5 grains) daily. In no single case was iodine dermatitis produced. As to the efficacy of an iodine preparation in tertiary syphilis, Sommerville considers that its effect on gummata is decisive. In this respect iodival proved very useful in many cases. After commencing the iodival treatment the growth of the gummata ceased, they were absorbed, and in favourable cases disappeared after 3 or 4 weeks without leaving a trace. In obstinate chronic ulcers the only improvement observed was the checking of their further spread.

v. Notthafft states, as the result of his experience, that iodival may cause iodism in the nervous system. Since it has been shown that iodival is deposited in considerable quantity in the nervous system, the author is not surprised at this action. For this reason he does not consider the preparation suited for the treatment of syphilis of the nerves.

E. Bröking found that no appreciable liberation of iodine from iodival was produced by gastric and intestinal digestion. The elimination of iodine begins just as soon as with potassium iodide, and amounts to about 80 p.c., as with the latter. In a unit of time its elimination is more uniform than is the case with potassium iodide.

F. Bönning used iodival with satisfactory results as a substitute for the alkaline iodides in arterio-sclerosis, asthma, bronchitis, apoplexy, pleurisy, osteomyelitis, optic nerve atrophy and syphilitic coxitis.

### **Iodoglidine.**

This remedy\*) has been prescribed by v. Notthafft in a large number of cases of syphilis. On the whole he was satisfied with its action. In tertiary syphilis and headache due to syphilis it gave good results, although it seemed

v. Notthafft, Monatshefte für praktische Dermatologie 1910, Vol. 51, No. 8, p. 344.

Bröking, Zeitschrift für experimentelle Pathologie und Therapie 1910, Vol. 8, No. 1.

Bönning, Medizinische Klinik 1910, No. 49.

\*) See Merck's Reports 1907 and 1908.

Notthafft, Monatshefte für praktische Dermatologie 1910, Vol. 51, No. 8, p. 343.



to act rather more slowly than the alkaline iodides. For this reason the latter are to be preferred to iodoglidine for headache and threatened tertiary conditions. With regard to the tolerance of patients for iodoglidine, it is somewhat better tolerated than the alkaline iodides, this opinion being founded rather on general impression than on absolute numerical data, for the alkaline iodides agree very differently with different persons, and we know from experience that one patient will stand large doses while another shows signs of iodism after small doses. The same was found by Nottthafft to be the case with iodoglidine. On the whole less disturbance is observed than when potassium iodide is used, though it occurs not infrequently that sensitive stomachs are upset by it, dyspepsia may set in, and may last for days or weeks, and hyperacidity and irregular action of the bowels may occur. Iodine coryza was frequently observed, iodine acne repeatedly. The doses of iodoglidine were not particularly large; the symptoms might set in within seven days, after taking no more than 24 tablets (containing 0.5 gramme of iodoglidine = 1.2 grammes of iodine). In another case the very large amount of 810 tablets, given within 3 months, was borne without injury. The author mentions two cases which show, in opposition to the statements of other authors, that iodism may occur on the use of iodoglidine even in persons who had previously stood the alkaline iodides without ill effects, and this although quite ordinary doses of iodine were given. Nottthafft will not allow that the secondary effects of iodoglidine in these cases could be justly attributed to idiosyncrasy.

### **Iodomenin.**

E. Gumbert, in estimating the value of iodomenin\*) in arterio-sclerosis, found that it was almost invariably well tolerated, and produced an improvement which showed itself not only in a reduction of the subjective conditions, but also objectively, e. g., in the condition of the heart, the blood pressure, etc. In one case of disturbance of compensation only did it fail completely. Gumbert, like Friedmann, states that with iodomenin the same results may

Gumbert, *Therapie der Gegenwart* 1910, No. 2.

\*) See Merck's Reports 1909, p. 243.

Friedmann, *Berliner klinische Wochenschrift* 1909, p. 500.

be obtained with far smaller doses than with potassium iodide. He attempts to prove this fact by quoting a case of arterio-sclerosis following syphilis in which a gumma, which was present at the same time on the right leg, closed without other treatment after giving 2 tablets of iodomenin 3 times a day. In another case of arterio-sclerosis after syphilis, in which a slightly positive Wassermann reaction had been obtained, the reaction disappeared after 3 months' use of iodomenin. As to the administration of the preparation, it must certainly be taken for considerable periods if its action is to be fully manifested. It is best to allow an interval of 8 to 14 days in each month, or else to leave off its use for a considerable time after several weeks.

Whether iodomenin passes through the stomach unchanged as some have asserted, is doubted by K. Taege by reason of his chemical investigations. He found iodomenin to contain 4.45 p.c. of iodine combined with albumin. Nearly 75 p. c. of its iodine content is present in an inorganic form, which may for the greater part be readily extracted with water. The author is therefore of opinion that iodomenin cannot possess any considerable advantages over potassium iodide with its content of 76.4 p.c. of iodine.

### **Iothion.**

Where there is an idiosyncrasy for internal iodine preparations, iothion appears, from the reports of P. Piericcuoli, to be especially well suited as a substitute, for when given percutaneously it is very rapidly absorbed. The author found that after rubbing 3 grammes (45 grains) of 30 p.c. iothion ointment into the skin iodine could be detected in the urine and in the saliva after 20 minutes. In the urine the presence of iodine could be demonstrated 70 hours after application. The author was also able to show in syphilitic subjects that the use of iothion led to a slow increase of the hæmoglobin in the blood, with a slight reduction in the leucocytes. No harm is done to the skin or to the organism by iothion treatment, at any rate the

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Taege, *Medizinische Klinik* 1910, No. 39.

Piericcuoli, *Rivista medica pugliese* 1909, No. 12. — *Monatshefte für praktische Dermatologie* 1910, Vol. 51, No. 9.

author has observed nothing more than the occurrence of a slight burning sensation and transitory reddening of the skin.

H. Leyden tried iothion with good results in gynæcological cases. He prescribed gelatin globuli of the following composition: About 11 grammes of gelatin are dissolved in 100 grammes of anhydrous glycerin by the aid of heat. 5 grammes of iothion are added to this solution warmed to 35—40° C., and globuli are prepared from it by pouring the solution into suitable moulds. These are introduced at night. In the author's experience this gave the best results in fluor albus, which disappeared after 4 or 5 weeks' treatment. They were also useful in inflammation of the ovaries and, when used for a prolonged period, in erosions of the cervix. Another indication for iothion is given by Leyden, viz., catarrh and swelling of the nasal mucous membrane. In this case he used a mixture of 5 parts of iothion with 95 parts of glycerin, which he applied as a paint. This led to the rapid disappearance of the difficulty in breathing, while it accelerated the recovery. Equally good results were obtained by A. Mühsam with iothion in laryngological practice. He used a 4 p.c. solution of the mixture with glycerin in place of Lugol's iodine solution, and he states that he obtained the same effect as with the iodine solution. The iothion-glycerin mixture is said to have the advantage of being colourless, and is free from the unpleasant taste of iodine. For the treatment of moist eczema of the skin Leyden recommends a trial with a mixture of 2.5 grammes of iothion, 10 grammes of absolute alcohol and 37.5 grammes of anhydrous glycerin, for in one case he obtained a cure in a few days. Iothion appears to be suited for the purpose of disinfecting the skin. K. Witthauer thoroughly cleanses the field of the operation by means of lysoform-alcohol, and then paints it several times with a 12 p. c. alcoholic solution of iothion which rapidly penetrates into the skin. After the operation the margins of the wound are rubbed with iothion solution before suturing. With this method of administration Witthauer observed inflammation of the skin in one case.

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Leyden, *Therapeutische Monatshefte* 1910, No. 2.

Mühsam, *Therapie der Gegenwart* 1910, No. 11.

Witthauer, *Medizinische Klinik* 1910, No. 31.



The disinfectant action of iothion led Memelsdorf to prescribe it in dentistry in place of tincture of iodine in gingivitis and stomatitis. In periostitis it is also said to be of good service. As a paint he uses a mixture of 5 grammes of iothion, 3 grammes of glycerin and 2 grammes of alcohol. This is mixed with equal parts of zinc oxide, when it may be used as a paste. As special advantages of the iothion solution the author mentions that it is colourless and has a deep action without harming the gums. He points out, however, that the solution does not keep long. It should therefore be prepared fresh for use.

In children C. Stamm tried a 10 p.c. iothion ointment, and in swollen glands, parenchymatous enlargement of the thyroid before puberty, and in mastitis adolescentium he obtained satisfactory results.

Iothion may also be given per rectum with advantage. G. Wesenberg showed that it is very quickly absorbed from the large intestine. He therefore recommends it in the form of suppositories containing 0.15 to 0.25 gramme of iothion and 2 gramme of cacao butter.

In veterinary practice, in place of iothion, a 25 p.c. vasoliment containing iothion is suitable. It is called iothionol. Schindler found it indicated in galls of the extensor and flexor tendons, of the hock, in cellulitis, sclerodermia and in the after treatment following the extirpation of breast boils, swelling of the spermatic cord or other tumours remaining after wounds; it is applied by rubbing.

### **Isoform.**

A dry treatment of gonorrhœa in women has been suggested by R. Asch, in which isoform\*) takes the chief part as a curative and disinfectant agent. The preparation is said by the author to be particularly suitable as a permanent antiseptic, and this is absolutely necessary for the cure of gonorrhœa of mucous membranes. For the self-treatment of urethral gonorrhœa he recommends, instead of injections,

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Memelsdorf, Zeitschrift für Zahnheilkunde 1910, No. 3.

Stamm, Therapeutische Monatshefte 1910, No. 12.

Wesenberg, Deutsche medizinische Wochenschrift 1910, No. 46.

Schindler, Berliner tierärztliche Wochenschrift 1910, No. 48.

Asch, Zentralblatt für Gynäkologie 1910, No. 12.

\*) See Merck's Reports 1905 and 1906.

the use of isoform bougies containing 5, 10, or 20 p.c. of isoform. One of these is introduced into the urethra twice a day. In urethro-vaginitis infantum the bougies are placed in the vagina, one every 3 to 4 days. Urethral gonorrhœa can only be treated with lasting success when cervical and uterine gonorrhœa has been cured, and inversely. Otherwise it is not possible to prevent reinfection. Asch therefore plugs the vagina with 5 or 10 p.c. isoform gauze. A tampon may be left as a rule 2 to 4 days before it need be removed. The author has treated 125 cases exclusively with isoform. Of these 56 were cured after treatment for 3 to 4 weeks, and 20 after more prolonged treatment. In 15 patients an improvement only was obtained, as they had been unable to carry out the treatment with sufficient regularity. In a few cases only did isoform produce inflammation.

### Iron Sajodin.

Under the name of "iron sajodin" is issued the basic iron salt of iodo-behenic acid. It is a reddish-brown amorphous powder, with scarcely any taste or smell. It is soluble in ether, benzol and chloroform, but insoluble in water and alcohol. It is also soluble in fatty oils and is therefore well suited for the preparation of ferrated and iodised cod liver oil. The preparation contains 5.6 p. c. of iron and 25 p. c. of iodine. A tablet of iron sajodin of 0.5 gramme ( $7\frac{1}{2}$  grains) is thus equivalent to 0.12 gramme (2 grains) of iodine and 0.03 gramme ( $\frac{1}{2}$  grain) of iron.

Görges found that iron sajodin is well absorbed, though it is split up and eliminated more slowly than the alkaline iodides or the iodide of iron in syrupus ferri iodidi, and for this reason it is particularly valuable in the treatment of chronic diseases. The author's observations have shown, up to the present, that it is suitable in the treatment of congenital syphilis in children where there is a deficiency of hæmoglobin, and for anæmic and chlorotic children with scrofulous diseases such as swollen glands or eczema. In general the new preparation is indicated wherever metabolism is retarded by disturbed nutrition in the above-named diseases. The remedy is well tolerated even on prolonged use, hence it is also indicated in arterio-sclerosis with anæmia. The

action of the preparation is very soon apparent in scrofulous children, the first effect being an increase in appetite and a gain in weight. This is followed by a disappearance of the symptoms and an improvement in the appearance and general condition. No unpleasant secondary effects were ever seen by the author in the children treated with iron sajodin, though in adults iodism occurred in exceptional cases. Children are given  $\frac{1}{2}$  to 1 sajodin tablet 3 times a day; adults may be given as many as 6 tablets daily. J. Ruhemann also obtained satisfactory results with iron sajodin treatment. In addition to the above named indications the author used it with success in fatty heart, Graves's disease, general obesity, chronic parametritis, dysmenorrhœa and arterio-sclerosis.

Like Görges, P. Cohn also found that iron sajodin has a good effect on the general condition in various scrofulous affections of the eye. The action of the remedy on the disease of the eye, except in obstinate cases, was beyond doubt.

A communication on the use of iron sajodin in rhinolaryngological practice has been published by E. Meyer. He found the remedy to be of good service in laryngitis nodosa in children, in goitre and in bronchitis.

Two new preparations obtained with iron sajodin and their therapeutical use are described by O. Lehmann: One is an iron sajodin emulsion, 10 c. c. of which contain exactly 0.02 gramme of iodine and 0.008 gramme of iron. It is used where it is desired to give iodine and iron with but little oil, e. g., in the plethoric form of scrofula. The other preparation is an iodine-iron cod liver oil, i. e., a solution of iron sajodin in cod liver oil containing the same amount of iodine and iron as in the emulsion already mentioned. The remedy is indicated where it is desirable to administer fat in addition to iodine and iron. 5 to 10 c. c. are given 3 times a day, according to the age of the children.

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Ruhemann, Deutsche medizinische Wochenschrift 1910, No. 37, p. 1714.

Cohn, Medizinische Klinik 1910, No. 42, p. 1654.

Meyer, Berliner klinische Wochenschrift 1910, No. 42.

Lehmann, Allgemeine medizinische Zentralzeitung 1910, No. 40.



### Kamala.

A pharmacological paper on kamala, the anthelmintic and tænifuge that is largely used in veterinary medicine, has been published by A. Semper. His results show that the drug has a poisonous action on frogs, tadpoles, and earth worms, and it may be presumed that the poisonous action is due to substances contained in kamala which resemble chemically and physiologically the toxic substances contained in the filix root. At any rate, when frogs are given kamala the symptoms which lead to their death resemble those produced by poisoning with the various filix substances. The action of kamala on the nerves and muscles is also similar to that of the filix substances. A point of practical importance is the fact that the preparations obtained from kamala, rottlerin and the ethereal extract of kamala, possess the same qualitative action of the drug but not the same quantitative action, for the action of the drug is more powerful, and this may be due to the fact that kamala offers a larger surface to the alkaline intestinal juice, and is therefore more fully extracted. Consequently the kamala extracts should be given in appreciably larger doses than those corresponding to the proportions of the drug and the extract.

Trials on dogs have shown that a single dose of kamala and its products gives rise to no demonstrable absorptive effects. On repeated administration the author observed a local action of the drug in the intestinal canal, and also albuminuria.

### Kephaldol.

Communications by K. Lill show kephaldol\*) to be a trustworthy antipyretic. Defervescence takes place about an hour after its administration without unpleasant effects on the patients; occasionally an attack of sweating occurs. In typhoid fever the temperature may be kept at a comparatively low level for days, and the general condition as well as the heart's action may be improved. As a remedy for rheuma-

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Semper, Archiv für experimentelle Pathologie und Pharmakologie 1910, Vol. 63, p. 10.

Lill, Medizinische Klinik 1910, No. 50.

\*) See Merck's Reports 1909.

tism kephaldol is indicated in acute rheumatism and still more in chronic muscular rheumatism. It contributes to the disappearance of the inflammation and pain. In the various forms of neuralgia, in headache, in neurasthenia and anæmia and in the gastric crises occurring in arterio-sclerosis of the mesenteric vessels, kephaldol exhibits a prompt action. The dose of the preparation amounts to 0.5 to 1 gramme (7½ to 15 grains). As a rule 2 to 4 grammes (30—60 grains) are sufficient.

Ch. Busch also expressed himself very well satisfied with the action of kephaldol in headache.

### **Lenicet.**

Of late years a basic aluminium acetate has been introduced under the name of lenicet. This has already been described in these Reports (Merck's Reports 1905 and 1906). It has also been recommended in the treatment of gonorrhœa\*) in the form of a 10 p.c. ointment to which the name "bleno-lenicet" has been given. Recent communications by M. Dölling show that the 5 and 10 p.c. bleno-lenicet ointments have yielded excellent results in ophthalmia adulatorum and neonatorum. In inflammation of the conjunctiva with profuse discharge, in inflammation of the edges of the lid and in catarrh with swelling, the preparation is said to be of good service. Spiro, however, reported an unsuccessful case of ophthalmia neonatorum treated with the ointment. H. Bayer and Kümmell then tested bleno-lenicet ointment more carefully, and both authors obtained very unsatisfactory results. Bayer was led by his results to doubt seriously whether treatment with this ointment was a safer method than silver treatment. Not only does the introduction of the ointment fail to protect the cornea, it does not exhibit the striking action on the discharge that others have spoken of. A point of special importance is the fact that the gonococci survived for a long time under

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Busch, Allgemeine medizinische Zentralzeitung 1910, No. 12.

\*) See Adam, Merck's Reports 1907, p. 159.

Dölling, Therapeutische Monatshefte 1910, No. 5, p. 280.

Spiro, Münchener medizinische Wochenschrift 1909, No. 34, p. 1735.

Bayer, Münchener medizinische Wochenschrift 1910, No. 19, p. 1010.

Kümmell, Münchener medizinische Wochenschrift 1910, No. 28, p. 1502.

treatment with the bleno-lenicet ointment, so that for this reason the author was obliged to return to silver treatment in a number of cases. On the whole Bayer considers that his bad results justify him in uttering a direct warning against the use of the ointment. Kümmell has also ceased to use lenicet ointment, which he prescribed formerly, though only for slight cases. He found that the results obtained with the ointment could not compare with those following the use of silver nitrate. His results may be considered free from objection, because he made his comparative experiments on the two eyes of the same person, and saw that the eye treated with ointment, when compared with the control eye as to the subsidence of the swelling and discharge, was distinctly less benefited, and the bacteria remained so long in this eye as to expose it to considerable danger.

### **Leucofermantin.**

E. Müller considers that the physiological treatment of suppuration should fulfil a double duty. Firstly it should enable the natural curative and protective powers of the organism to carry out their functions to the full, or to be increased, and secondly it should reduce the fermentative efforts of the organism to a level serviceable for a cure, for the resisting powers of the body are injured by excessive efforts. While cold pus is poor in ferments, hot pus contains polymorphonuclear leucocytes which contain a proteolytic ferment in large quantities which resembles trypsin in its action. It is necessary therefore to convert hot pus to some extent into cold by the addition of antiferment, and thus to protect the tissues in contact with the pus from its power of dissolving albumin. It must also prevent the too rapid absorption of toxic albuminous products from the suppurating focus. Leucofermantin, which has already been described in these Reports, is suitable for antiferment treatment, and has already been shown by a number of authors\*) to yield good results in the treatment of suppuration. Müller found that the temperature fell at once, and the œdema subsided

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Müller, *Münchener medizinische Wochenschrift* 1910, No. 16, p. 883.

— *Medizinische Klinik* 1910, No. 14, p. 562.

\*) See Merck's Reports 1908 and 1909.



rapidly, while the commencing softening was checked very quickly, the purulent discharge ceased, and fresh, healthy granulations sprang up and led to rapid and sharp limitation of the tissue necrosis.

D. MacEwan treated 15 cases of acute suppuration with leucofermantin, and, except in two cases, obtained very satisfactory results. After emptying the abscesses by aspiration with a fairly wide needle, he injected 2 to 15 c.c. of leucofermantin, according to the size of the abscess, and applied an antiseptic dressing. With this treatment the abscess healed more quickly than with the usual methods. In the aspirated cases the abscess healed without leaving a scar. The author is therefore of opinion that the preparation, in addition to its antiproteolytic properties, has also bactericidal and other protective properties. The reports of J. Nosek show that leucofermantin may be of good service in the treatment of hot abscesses.

Hesse also made a thorough examination of the value of leucofermantin, and of 26 cases he obtained very favourable results in 19. In large abscesses he opens the abscess, removes the pus and fills the cavity with leucofermantin to the amount of a third of the evacuated pus. The wound is then sewn up at once. The small dose of leucofermantin has the object of putting no strain on the fresh suture. Its action is sufficient, for the temperature falls and the pains subside very promptly, and the abscess soon heals. The chief result of his investigation culminates in parallel experiments in which he found that cases treated with leucofermantin heal in 6 days, while those not treated with it require 14 to 18 days to heal. Anaphylaxis, as observed by Brüning, never occurred in the author's cases. Even large abscesses may be healed in a short time by this method, although Gergö holds a contrary view.

A surprisingly prompt action of leucofermantin is reported by W. Hannes, who used the remedy in a para-urethral

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MacEwan, *British Medical Journal* 1910, No. 2560, p. 185.

Nosek, *Casopis lékařů českých* 1910, No. 36.

Hesse, *Archiv für klinische Chirurgie* 1910, No. 1.

Brüning, *Deutsche Zeitschrift für Chirurgie*, Vol. 10.

Gergö, *Deutsche Zeitschrift für Chirurgie*, Vol. 10.

Hannes, *Zeitschrift für gynäkologische Urologie (Leipzig)* 1910, Vol. II, No. 4.

abscess. He punctured the abscess from the vagina by means of an aspiration syringe, evacuated the pus and injected enough leucofermantin to fill the cavity fairly tensely. From the following day the patient was free from fever, and was able to urinate spontaneously without trouble. After 3 days the tumour had disappeared, and the patient could be given antigonorrhoeal treatment.

E. Bircher used leucofermantin first in deep fistulæ left after drainage in peritonitis, and which in consequence of a rupture of the intestine extended to some depth and showed little tendency to heal. By plugging with strips soaked in leucofermantin they healed in the course of 4 days. An equally good result was obtained with leucofermantin in suture fistulæ following operations on the thyroid, and in all wounds which showed little tendency to heal. The author also tried leucofermantin after appendicectomy, for he was convinced that the peritoneal exudation following the operation contained toxins and proteolytic ferments which were to blame for the rise of temperature which continues for days after operation, as occasionally a paralytic ileus also leads to tedious operative after treatment. For this reason the author treated 35 cases of acute appendicitis, complicated with severe peritonitis in 5 cases, by removing the appendix and then emptying the contents of a bottle of leucofermantin into the abdominal cavity in gangrenous appendicitis, or of two bottles in perforation and peritonitis. Bircher states that there is no need to wash out the abdomen, it is sufficient to remove the discharge by swabs and to pour the leucofermantin, warmed to 20° C., into the abdominal cavity shortly before closing the wound. In cases with suppuration he introduced a rubber drainage tube into the peritoneum. The whole of the 35 cases yielded excellent results. Those with well marked peritonitis reacted almost as promptly to leucofermantin, and the temperature always fell after 3 to 4 days. As the result of these successful cases the author believes that leucofermantin may be recommended, though he points out that the preparation must not be regarded as a universal remedy for peritonitis.

M. Hirsch found that circumscribed foci of suppuration could be cured by antiferment treatment, but not

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Bircher, *Medizinische Klinik* 1910, No. 26.

Hirsch, *Berliner klinische Wochenschrift* 1910, No. 13.

progressive suppuration. His observations differed from those of other authors, for he found that healing took longer with antiferment treatment after puncture than with the regular surgical treatment by incision, as reported above. Hesse also preferred incision of abscesses to puncture.

### Limonene.

Limonene was recommended by Kobert some time ago as a substitute for oil of turpentine, and G. Zickgraf has recently drawn attention to this preparation. Limonene is a terpene contained in many essential oils ( $C_{10}H_{16}$ ). It is usually obtained from the essential oil of orange peel or from oil of caraway. The preparation is clear, like water, is optically active and has an odour resembling that of oil of lemon.

Zickgraf found it indicated in all conditions in the lungs coupled with offensive expectoration, in which oil of turpentine has hitherto been used, also in foetid bronchitis, foetid bronchiectasis, gangrene of the lung and tuberculous cavities. In the author's experience limonene is superior to oil of turpentine, not only in having an agreeable odour but also in being apparently more efficacious. At first the author used the remedy by inhalation only, but he soon proceeded to administer it internally in addition to the inhalation method, having been convinced by experiments that the preparation does not give rise to albuminuria. It may be given without harm 3 times a day in doses of 10 to 20 drops on sugar or in water.

Limonene gave excellent results in foetid expectoration, the offensive smell being abolished after a few days. The sputum was also reduced in quantity by limonene treatment, and the profuse secretion diminished considerably or disappeared altogether. In place of natural limonene Zickgraf says that the artificial product may be used\*).

Limonene is also used as a stomachic, as an addition to sleeping draughts, as a corrective to the smell of antiseptics, and for the conservation of oleum phosphoratum\*\*).

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Kobert, Intoxikationen 1906, II., p. 134.

Zickgraf, Münchener medizinische Wochenschrift 1910, No. 20, p. 1070.

\*) See O. Schweissinger, Pharmazeutische Zentralhalle 1902, p. 260.

\*\*) Also issued under the name of "Eulimen".



**Liquid carbon dioxide.**

Liquid carbon dioxide is found useful in many small industries, and is comparatively easy to produce. It has now been used therapeutically. It is well known that liquid carbon dioxide may be made to escape from the steel cylinders in which it is supplied commercially in such a way that solid carbon dioxide is readily formed. This so-called carbon dioxide snow changes very slowly into the gaseous state. Its temperature is so low that it may produce inflammation of the skin in a way which exactly resembles the appearances of a burn. If carbon dioxide snow is pressed upon the skin, this becomes almost insensitive at once, and after 30 to 60 seconds a blister forms (resembling the blister of a burn). This suggested the idea of using solid carbon dioxide to produce anæsthesia by cold, as has been customary for a long time by the use of ethyl chloride. G. Malan carried this idea into practice. To produce the local anæsthesia necessary for operations, carbon dioxide snow need only be applied to the skin for 5 to 8 seconds. The incision, as for furuncles, must be made at once, for the anæsthesia lasts but a very short time. Malan tested it in furuncles, abscesses, anthrax, buboes and cellulitis, and he found the anæsthesia sufficient and deeper than that produced by ethyl chloride.

W. S. Gottheil successfully treated 3 cases of lupus erythematosus by the carbon dioxide freezing method. The carbon dioxide snow may be readily pressed into any desired form, and it may be made into a stick with which the lupus patches are treated for 20 to 60 seconds. The severity of the reaction depends not only on the duration of the action but also on the pressure with which the preparation is applied to the spot. The destruction of tissue takes place without pain, for the carbon dioxide, as already stated, has an anæsthetic action. The author therefore regards this method as the best known way of treating lupus. This is confirmed by M. Serano and J. Nouell. These authors extend the field of utility of carbon dioxide to superficial epitheliomata, tuberculous lupus and ordinary warts and cica-

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Malan, *Gazzetta degli ospedali e delle cliniche* 1910, No. 105.

Gottheil, *New York Medical Journal* 1909, 3<sup>rd</sup> July.

Serano - Nouell, *Monatshefte für praktische Dermatologie* 1910, Vol. 50, No. 7.

tricial keloid tissue. The treatment of warts and nævi with carbon dioxide is also described by W. Allen Pusey, J. M. H. Macleod and J. Fabry and Zweig. Macleod mentions 30 seconds as the longest time for the application of carbon dioxide snow to nævi. Longer applications may produce inflammation and disfiguring scars. In rodent ulcer and warts, however, the remedy should be allowed to act for at least a minute, to make sure that the tissue is really destroyed. The author has used the method especially in vascular nævi in children with excellent results. Fabry and Zweig show that the treatment should not be extended beyond a minute for fear of necrosis when dealing with warts and corns.

Klotz used carbon dioxide snow with good results in the removal of exuberant granulations, and in cutaneous and subcutaneous tuberculides when readily accessible. Granulations of all kinds, especially those at the opening of tuberculous fistulæ, are said by the author to heal under carbon dioxide freezing as well as when cauterised with silver nitrate. This treatment has the further advantage of being painless as compared with curetting with a sharp spoon. The author obtained particularly good results in subcutaneous tuberculides. The treatment is less promising in tuberculous glands in the neck, for in this case the treatment must be very energetic, and consequently painful. The ideal and safe method of dealing with small telangiectases is to destroy the vascular knots with carbonic acid.

### **Liquor calcis.**

In a case of multiple warts (*verruca plana*) Dudley Kennard obtained such surprising results with lime water that he recommends this harmless remedy for further trial in suitable cases. He reports the case of one patient, the backs of whose hands were closely covered with small warts which refused to yield to local treatment by various remedies, or to internal treatment with calcium chloride, calcium iodide,

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Pusey, *Journal of cutaneous diseases* 1910, June. — *Monatshefte für praktische Dermatologie* 1910, Vol. 51, No. 7.

Macleod, *British Medical Journal* 1910, No. 2561, p. 254.

Fabry-Zweig, *Münchener medizinische Wochenschrift* 1910, No. 13.

Klotz, *Berliner klinische Wochenschrift* 1910, No. 48.

Kennard, *British Medical Journal* 1910, No. 2558, p. 81.

magnesium sulphate or arsenic. X ray treatment and scraping produced merely transitory success, for new warts continually appeared. Not until the author used lime water was a comparatively rapid cure obtained. He ordered her half a pint of lime water a day for a week. In the course of four days all the warts disappeared and did not return after months.

### **Magnesii carbonas.**

In the treatment of burns dry dressings have won much favour of late years. It is therefore important to draw attention to a remedy which is said by Ohleyer to be of very good service for dry dressings, and which is, as a rule, easily obtainable, viz., carbonate of magnesia. The author reports the case of a burn of the third degree in which he used the following treatment. Morning and evening the wound was thickly covered with powdered magnesium carbonate; this was covered with a double layer of gauze, and then with wool. The whole was fixed with bandages, using slight pressure. On renewing the dressings the portions of the dressing which adhered were first removed by swabbing with wool dipped in 0.1 p.c. lysol solution. The good results thus obtained are principally attributable to the dry treatment as such, and also to the alkalinity of the magnesium carbonate, for the muscle acids are neutralised and absorbed by it, while it prevents the pus from exercising a macerating action on the healthy skin.

### **Magnesii chloridum.**

This salt is little used in therapeutics and attention to it is drawn in a paper by Chibret. He considers that its use has been abandoned without proper reason in favour of other magnesium salts, such as the sulphate and citrate, for it is an ideal laxative. The author's observations show that magnesium chloride stimulates the intestinal muscles, regulates peristalsis, favours secretion, and acts as a tonic both to the digestive tract and the nervous system. Very frequently small doses of 0.05 to 0.25 gramme ( $\frac{3}{4}$ —4 grains)

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Ohleyer, *Ärztliche Rundschau* 1910, p. 433.

Chibret, *De l'emploi thérapeutique du chlorure de magnésium.*

Thèse de Paris 1910. — *Revue de thérapeutique* 1910, p. 646.



internally, or 0.25 to 4 grammes (4—60 grains) rectally, display an excellent action in atonic or spastic constipation. As a rule the author used it in constipation, for instance in membranaceous colitis, coprostasis, dyspepsia, chronic enteritis, affections of the liver, and various sequelæ of intestinal diseases (e. g., chronic catarrhal asthma). He gave 3 to 10 grammes (45—150 grains), which usually produced the desired purgative action, though it never caused colic, and, a point of particular importance, it never led to subsequent constipation, a well known effect of most laxatives.

It should be remarked that in the communications of Canestro Corrado, magnesium chloride is shown to be of use when administered by subcutaneous injection in tetany in place of the sulphate.

### **Magnesii sulphas.**

The use of magnesium sulphate as an anæsthetic has been described during the past year by Canestro Corrado, Schlewellyn Phillips, E. Johnson, P. Paterson and C. Canestro.

Canestro Corrado applied magnesium sulphate or magnesium chloride by subcutaneous injection. He injected suitable doses of a solution of 7.3 grammes in 100 grammes of water, and was able to deal successfully with tetanic symptoms following thyroidectomy. Paterson also gave subcutaneous injections of magnesium sulphate in a case of tetanus with the result that the pain diminished at once, and ultimately a cure was obtained, but he found the injections of magnesium sulphate to be very painful. He used 10 p.c. solutions, and injected 10 c.c. in the course of two days, giving small injections every four hours. Later he injected 20 c.c. more in small doses extended over 4 days.

Johnson used magnesium sulphate in 25 p.c. solution, applying it intraspinally after potassium bromide and chloral

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Corrado, *Il Policlinico* 1910, p. 124.

Canestro Corrado, *Revue de thérapeutique* 1910, No. 16, p. 556.

Schlewellyn Phillips, *Klinisch-therapeutische Wochenschrift* 1910, No. 10, p. 263.

Johnson, *British Medical Journal* 1910, No. 2590, p. 457.

Paterson, *Lancet* 1910, No. 4518, p. 922.

Canestro, *Klinisch-therapeutische Wochenschrift* 1910, No. 19, p. 455.

hydrate had been used without success. At first he gave 45 drops of the solution simultaneously with tetanus serum, but finding this treatment had no lasting effect he proceeded to inject magnesium sulphate by itself. After each injection the muscles relaxed promptly. Schlewellyn Phillips also found intraspinal injections of magnesium sulphate more effective than tetanus antitoxin.

A number of earlier communications\*) have dealt with the anæsthetic action of magnesium sulphate, especially when used intraspinally, and the toxic action of the salt on the respiratory centre has not escaped the notice of investigators\*\*). C. Canestro tried to prevent the inhibitory action of the remedy by using it in conjunction with a vaso-constrictor, and for this purpose he used adrenalin. His experiments on dogs showed that 0.02 gramme per kilogramme of body weight of a 25 p.c. solution of magnesium sulphate formed an excellent means of producing experimental spinal anæsthesia. On the addition of adrenalin the injection even of large quantities of magnesium sulphate, such as 0.06 gramme per kilogramme of body weight, caused no disturbance of respiration, although when no adrenalin was used a slight disturbance was produced. Complete anæsthesia and paralysis of the hind half of the body was obtained by the use of a weaker concentration, i. e., below 15 to 25 p.c., when adrenalin was added, while the same solution without adrenalin produced only a high degree of paresis with almost complete loss of sensibility. Hence adrenalin appears to have a good effect on the anæsthetic action of magnesium sulphate, so that in dogs no appreciable change in the general condition is produced. Thus the author was able to keep a dog alive in which he had injected by lumbar puncture 0.2 gramme of a 25 p.c. solution of magnesium sulphate per kilogramme of body weight, adrenalin having been added to it. It is true long-continued artificial respiration was necessary. However, a dose of 0.3 gramme per kilogramme of body weight proved fatal. In most of Canestro's experiments 2 drops of the ordinary adrenalin solution were added to each c.c. of magnesium sulphate solution. The author ascertained further that

\*) See Merck's Reports 1906—1909.

\*\*) See Page, *Klinisch-therapeutische Wochenschrift* 1910, p. 263.

the spinal anæsthesia produced by magnesium sulphate caused no changes in the central nervous system such as have been observed to follow the use of other anæsthetics. Neither were histological changes found in the kidney substance.

Attention must be drawn to a paper by H. F. Hyndham and W. E. Mitchener, who proved by animal experiment that magnesium sulphate injections paralysed only the sensory cells, but not the motor cells of the cerebral centres.

### Magnesium-Perhydrol.

The action of magnesium peroxide in attacks of stenocardia (in pseudo-angina pectoris and true angina pectoris) has been reported on by F. v. Chlapowski at the 31<sup>st</sup> meeting of the Balneological Society of Berlin. The author's patients consisted almost exclusively of elderly men (over 50 years of age) with arterio-sclerosis, who had come to Bad Kissingen for treatment. The author prescribed special diet, iodine preparations, and magnesium peroxide, the latter in doses of 0.5 gramme ( $7\frac{1}{2}$  grains) after meals. The results show that it was excellently tolerated as a rule, for oppression, pyrosis, fear and pain subsided very quickly, and the peroxide did away with the need for the use of nitroglycerin. Even in a very severe case in which the patient died from an apoplectic seizure 3 weeks after the beginning of the treatment, the preparation was of good service. The action of magnesium peroxide is due in part to its power of neutralising the excess of gastric acid, in part also to the relief of constipation, and more especially to the reduction of abnormal gas formation. The author does not express an opinion as to whether magnesium peroxide has an additional sedative action on the circulation or the nervous system, or whether the oxygen liberated from the peroxide has a special action.

Excellent results were obtained by F. Poly with perhydrol in hyperchlorhydria. He gave his patients 300 c.c. of a 0.5 p.c. solution with a test breakfast roll on an empty stomach every other day. This treatment was repeated

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Hyndham - Mitchener, Journal of the American Medical Association 1910, 23<sup>rd</sup> July.

Chlapowski, Medizinische Klinik 1910, No. 23, p. 904.

Poly, Archiv für Verdauungskrankheiten 1910, Vol. 16, p. 700.



according to the effect obtained. When the increase of acidity was slight 3 to 5 doses sufficed to relieve pain which was very severe in some cases, while a high degree of hyperchlorhydria required 10 to 14 doses. The results both in relieving the pain and in correcting the acid were extraordinarily good. In the obstinate and severe cases of hyperchlorhydria especially, the remedy stood the test brilliantly, and always produced the desired result when correctly used. The author used perhydrol to make his trials as free from objection as possible, though he considers magnesium-perhydrol to be more agreeable to the patients, and very well suited for therapeutic purposes.

The large amount of peroxide contained in magnesium-perhydrol makes it of importance in the treatment of diabetes. C. von Stürmer tried it with the result that doses of 0.5 gramme ( $7\frac{1}{2}$  grains) of magnesium-perhydrol given 3 times a day reduced the sugar in the urine to a minimum, without observing any special diet. The urine also becomes alkaline under this treatment, and the acidosis which is a common forerunner of diabetic coma is relieved.

H. Günther describes a reaction for bilirubin in the urine characterised by simplicity of execution and by great sensitiveness. His directions are as follows: About 5 c.c. of glacial acetic acid are added to a small quantity of magnesium-perhydrol Merck (not more than 0.005 gramme) and this is heated to boiling in a test tube. To this reagent a few drops of dark icteric urine are added, after having been made strongly alkaline by the addition of caustic soda. In the case of a pale, alkaline urine 5—10 c.c. are added. In the presence of bilirubin a green colour appears immediately after the addition of the urine, or after heating the mixture again for a short time. A positive reaction is obtained if the urine contains bilirubin in the proportion of 1:100,000. The green colour is said by the author to turn blue on the addition of hydrochloric acid. The green colouring matter is soluble in chloroform, and is thus distinguished from biliverdin and biliprasin. When the colour produced is ill-defined, the mixture may be shaken up with 1 to 2 c.c. of chloroform, and the reaction thus made more definite.

Stürmer, *Münchener medizinische Wochenschrift* 1910, No. 49.  
Günther, *Medizinische Klinik* 1910, No. 27, p. 1056.

**Mastich.**

W. v. Oettingen recommended years ago mastich dressings for the treatment of wounds. He now gives an account of his further experiences. As already known he used a solution of 20 grammes ( $\frac{2}{3}$  oz) of mastich in 50 grammes ( $1\frac{1}{4}$  oz) of chloroform and 20 drops of linseed oil to fix the dressings, a method which he worked out in the Russo-Japanese war with especially good results, when there was no water for cleaning the hands. The method is worthy of universal attention for the treatment of wounds, and not only in military surgery, for mastich dressings have the advantage over painting with iodine that they adhere to the surface, and by keeping away moisture prevent the growth of bacteria. It forms a substitute for cleansing the neighbourhood of the wounds, for when the chloroform evaporates a layer remains on the skin of the field of the operation, and this fixes the pathogenic bacteria present on the skin, and also fixes the wool or gauze dressing applied to the wound. The author has recently suggested for this purpose a plug of wool consisting of four layers of muslin (16 x 16 cm.) containing a layer of cotton wool (9 x 9 cm.). 20 to 30 of these plugs are sterilised in parchment paper so that they can be taken out in a sterile condition. They are pressed upon the wound and are held in firm contact by a mastich solution that has been previously applied to the skin. The dressing is particularly suitable in cases in which bandages cannot conveniently be applied, or in which they are apt to be displaced, e. g., on the shoulder or on the back. This is confirmed by F. Thalwitzer who tried the method and found it very useful in minor surgery in his consulting room.

Mastich solution may be used with advantage for bandaging. F. Daxenberger found that he could instil drops into the eye or use other suitable treatment, and then place muslin, or cotton wool and muslin compresses over

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Oettingen, Deutsche Medizinalzeitung 1910, p. 134. — Münchener medizinische Wochenschrift 1910, p. 979.

\*) See Merck's Reports 1906.

Thalwitzer, Medico 1909, No. 51. — Excerpta medica 1910, p. 423.  
Daxenberger, Wochenschrift für Therapie und Hygiene des Auges 1910, Vol. 13, p. 329.

the eye, and fix them to the healthy dry skin of the forehead, cheek, nose and temple by means of mastich solution. These dressings also serve as a substitute for compresses, the drug being placed upon the dressing. The author considers this method better than the application of compresses, for there is no possibility of the eye being rubbed, and possibly infected by the hands. In applying the dressing care must of course be taken to prevent the mastich solution from flowing into the eye. On removing the dressing the dry mastich is softened by pledgets of wool soaked in benzin or chloroform.

We may safely assume that mastich solution will prove useful in orthopædic practice. Thus Muskat has recommended the use of mastich solution for dressings in place of adhesive strapping in affections of the feet, especially in flat foot. For details of his method, the author's original paper should be consulted.

### Menthol.

Menthol appears to have little effect in tuberculosis when given internally. Stepp therefore tried the percutaneous application of the preparation in the form of an ointment, and he obtained remarkable results. He used an ointment consisting of 12.5 grammes (187 grains) of menthol and 25 grammes ( $\frac{5}{6}$  oz) of anhydrous eucerin. This quantity was used in the course of 5 days. The ointment is rubbed into a different part of the skin every day for 10 minutes until the skin is almost dry. This treatment must be continued with energy and patience for 4 to 5 months or longer, for the success of the treatment depends upon its duration. The author describes 16 cases treated in this manner. One case in the first stage was cured (relatively) after a comparatively brief time; eight patients in the second stage were improved; of 7 patients in the third stage two showed no signs of disease, 3 showed considerable improvement, and 2 died of pneumothorax after there had been an objective improvement, and the dulness had cleared up. Acute tuberculosis and tuberculosis with diabetes are not improved by menthol treatment. External glandular tuber-

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Muskat, Archiv für Orthopädie, Mechanothérapie und Unfallchirurgie 1910, Vol. 8, No. 4.

Stepp, Klinisch-therapeutische Wochenschrift 1910, No. 24.



culosis and tuberculosis of the bones are not amenable to its influence. The action of menthol is ascribed by the author to its absorption by the lymphatic vessels of the skin, and subsequent elimination by the lungs, so that it acts on the chronically inflamed tissues of the lungs, causing their absorption.

In coryza in infants, von Mettenheimer recommends the use of an ointment to assist the mechanical cleaning of the nose, and to cause a reduction in the swelling of the mucous membrane. His ointment is composed as follows: Menthol 0.1 ( $1\frac{1}{2}$  grains), anæsthesin 1.5 (24 grains), adipis lanæ 15.0 ( $\frac{1}{2}$  oz), vaselin benzoat. (8 p. c.) ad 30.0 (1 oz). In infants the use of menthol preparations is not quite free from danger, as appears from a communication by W. Koch. The author painted the nose of an infant with coryfin (ethyl glycolic ester of menthol) for the relief of acute rhinitis. Dangerous spasm of the larynx was produced. This was clearly caused by the coryfin, for the child tolerated subsequent plugging of the nose without coryfin.

### Mergal.

C. Grünbaum sums up the opinions hitherto expressed\*) on mergal as follows: Mergal is equally useful for treatment by inunction and by injection. It may be given in large doses without harm; it is well tolerated by the digestive organs, causes no intestinal lesions, and does not give rise to colic and diarrhoea. The absorption of the mercury is uniform, rapid and proportional to the amount of mergal introduced. Mergal treatment is pleasant, convenient, cheaper than other methods, and may be carried out in detail under all conditions. Other observers have described unpleasant secondary symptoms such as gastric and intestinal disturbance. These can be prevented or at any rate reduced to a minimum by attention to diet, and by appropriate general regulations. In the treatment of syphilis with mergal the following points should therefore be observed:

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Mettenheimer, Zeitschrift für ärztliche Fortbildung 1910, No. 6.

Koch, Münchener medizinische Wochenschrift 1910, No. 37.

Grünbaum, Fortschritte der Medizin 1910, No. 50 and 51.

\*) See Merck's Reports 1906—1909.

It is advisable to take gruel and food containing flour, cocoa, and chocolate frequently. The following should be avoided: raw fruit, vegetables that cause flatulence, stewed fruits having an aperient action, acid and fatty foods, as well as pepper, mustard, horse-radish, coffee, tobacco and alcohol, a little red wine excepted. The mouth and teeth should receive most careful attention. For this purpose givasan tooth paste is the best preparation, and the teeth should be brushed with it after every meal. Care of the skin by warm baths assists the treatment.

The results obtained with mergal by Grünbaum are described as follows: Maculous exanthemata were as a rule cured after the use of 50 to 100 mergal capsules; papulous exanthemata disappeared after taking 100 to 150 capsules. Plaques on the mucous membrane healed in a few days, frequently after the use of only 20 to 30 capsules. Specific tonsillitis disappeared after 100 capsules on an average, but in tertiary syphilis 200 to 300 capsules were required for the complete disappearance of the symptoms.

Grünbaum as a rule prescribed 2 mergal capsules 3 times a day, and continued the treatment for at least 3 months.

K. Grön recommends mergal particularly where no very energetic mercurial treatment is considered necessary or advisable.

### **Methylene blue.**

A very simple method of staining diphtheria bacilli is described by P. Sommerfeld. The staining fluid is an aqueous or alcoholic solution of methylene blue, or the alkaline methylene blue solution of Loeffler\*). The method depends on the fact that the polar granules of the diphtheria bacilli retain the stain very firmly, and so differ from the bodies of the bacilli. The preparation is fixed and dried as usual, methylene blue solution is poured upon it, it is washed with water or dried with filter paper, and is then placed in a mixture of equal parts of alcohol and formaldehyde (40 p.c.) until it has become quite colourless, it is then washed with water and dried. Counter-staining

Grön, Norske Magazin for Laegevidenskaben 1910, No. 12.  
Sommerfeld, Deutsche medizinische Wochenschrift 1910, No. 11,  
p. 505.

\*) See Merck's Reagenzien-Verzeichnis 1908, p. 159.

is unnecessary, for perfectly clear and distinct slides are obtained. The polar granules appear dark blue, the bodies of the bacilli pale blue.

As a preliminary test for urine, to detect partial decomposition which might interfere with its further examination, Oefele recommends a reaction with methylene blue. If fresh urine is shaken up with methylene blue solution it becomes uniformly coloured, while decomposed urine becomes decolorised very soon from the bottom of the liquid, the decoloration extending upwards so that only the upper layer remains blue. Occasionally only a broad middle zone is decolorised. Whether this urine test is sufficiently definite in its significance requires further proof.

The use of methylene blue as an indicator in iodometric analysis is reported on by Frank Sturdy Sinnat. The author recommends, instead of starch solution, a solution of 0.05 gramme of methylene blue in 1000 c.c. of water. 1 c.c. of this is used for 50 c.c. of titration fluid. Iodine forms a compound with this stain, hence the slightest excess of free iodine causes the colour to change from blue to yellowish-green, and then to yellowish-brown. Methylene blue is said to have several advantages over solution of starch.

#### $\alpha$ -Naphthol.

The operative treatment of empyema occasionally gives rise to difficulty, for many medical men cannot undertake pleurotomy or thoracotomy, while in some cases this operation cannot be carried out. N. Maldaresku therefore worked out a method which is intended to take the place of the operation, or to be used in the after treatment. The method consists in the application of  $\alpha$ -naphthol injections. The pus should first be removed by aspiration; 10 to 20 c.c. of a 10 p. c. alcoholic solution of  $\alpha$ -naphthol are then injected into the pleural cavity. The action of  $\alpha$ -naphthol depends most probably on its bactericidal properties. As a rule a single injection suffices for a cure, but if this result is not obtained, the treatment may be repeated after

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Oefele, Pharmazeutische Zentralhalle 1910, p. 703.

Sinnat, The Analyst 1910, p. 309.

Maldaresku, Spitalul 1910, No. 10.



a few days. As a rule, however, there will be very little purulent discharge present that will require removal before the injection. In a number of cases of suppurative pleurisy the author obtained very satisfactory results by this method.

G. Goldschmiedt gives the following directions for testing urine for glycuronic acid: To 0.5 to 1 c.c. of urine 2 drops of a 15 p. c. alcoholic solution of  $\alpha$ -naphthol are added. This mixture is poured upon 3 to 4 c.c. of concentrated sulphuric acid. At the juncture of the layers a violet ring appears, and on standing it broadens towards the urine, while the sulphuric acid assumes a green colour from the juncture downward. On mixing the two layers a dark coloration appears, but this has nothing to do with the presence of glycuronic acid. The green colour may be obtained with a single drop of urine.

Another reaction for which  $\alpha$ -naphthol may be used is given by H. v. Wyss, E. Herzfeld and O. Rewidzow. If 4 drops of a 4.5 p. c. alcoholic solution of  $\alpha$ -naphthol, 4 drops of a 4.5 p. c. aqueous solution of sodium carbonate and 4 drops of a 4.5 p. c. alcoholic solution of p-phenylenediamine are added to 2 c.c. of pure amyl alcohol, an intense dark bluish-violet colour rapidly appears. The amyl alcohol appears to act in the same way as hydrogen peroxide. Iso-butyl alcohol gives the reaction in a far slighter degree.

### Nastin.

In a paper on the theory and practice of the treatment of leprosy with nastin, G. Deycke comes to the conclusion that benzoyl-nastin (nastin B) is a specific remedy which attacks the actual leprosy bacilli. By means of nastin treatment, provided it be carried out thoroughly and continued long enough, a large percentage of the cases may, in his experience, be more or less greatly improved as far as the leprosy symptoms and the general condition of the patients is concerned\*).

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Goldschmiedt, Zeitschrift für physiologische Chemie 1910, Vol. 65, p. 392.

Wyss-Herzfeld-Rewidzow, Zeitschrift für physiologische Chemie 1910, Vol. 64, p. 479.

Deycke, Monatshefte für praktische Dermatologie 1909, Vol. 49, No. 11, p. 475.

\*) See Merck's Reports 1907 and 1909.

J. Ashburton Thompson used nastin in 3 cases of tubercous and in one case of purely neurotic leprosy, and obtained no remarkable success.

### Neurine.

Neurine is so poisonous that it has not yet found its way into therapeutics, although it has been tried. It is known to be a constant product of the decomposition of dead bodies, but it may also be obtained synthetically, and is issued in a 25 p.c. aqueous solution. The chloride of neurine,  $C_2H_3N(CH_3)_3Cl$ , forms a yellowish, very hygroscopic powder which is very readily soluble in water.

The possibility of using neurine in bacterial diseases was dealt with in a paper by Roger and Josué, who found that neurine (and betaine) had the power of neutralising tetanus toxin, or at any rate of rendering it harmless. More recently, G. Deycke and H. Much have proved that neurine has a considerable bacteriolytic action. A 25 p.c. aqueous solution of the preparation dissolves tubercle bacilli as well as their granules at 37° C. in a few minutes. This discovery led the authors to try the use of neurine for dissolving tubercle bacilli for the purpose of obtaining vaccines. If this proves successful it would mark a material advance in the preparation of antigens, though the neurine would have to be removed from the resulting preparations, or at any rate rendered non-poisonous. The authors state that they have succeeded in the latter object; they state that all bacteria dissolve in neurine with the exception of anthrax bacilli, which merely swell up but are certainly killed.

### Neutralon.

A further communication by Th. Rosenheim and R. Ehrmann on the value and indications for neutralon\*) contains the following information:

Thompson, British Medical Journal 1910, No. 2566, p. 565. — Monatshefte für praktische Dermatologie 1910, Vol. 51, No. 2, p. 53.

Roger-Josué, Semaine médicale 1898, p. 141 and 486. — Merck's Reports 1898, p. 41.

Deycke-Much, Münchener medizinische Wochenschrift 1909, p. 1985 and 1910, p. 1094.

Rosenheim-Ehrmann, Deutsche medizinische Wochenschrift 1910, No. 3, p. 111.

\*) See Merck's Report 1909.

In all conditions of irritation of the secretory apparatus (hyperacidity, hypersecretion) whether primarily neurogenic or due to an organic cause, the preparation has frequently displayed a good effect on the course of digestion by reducing the acid and relieving pain. The results obtained in chronic hypersecretion were particularly favourable both in the alimentary and in the continued form coupled with more or less motor insufficiency. Objectively there was always found a diminution in the secretory activity, i. e., a reduction of the hyperacidity, and a diminution of the secretion of gastric juice in the fasting state. In these cases were included some in which neutralon occasionally gave relief when other drugs, particularly alkalies, had been used continuously with little or no benefit. Now and then the authors obtained a good effect with neutralon in general hyperæsthesia of the gastric mucous membrane due to anæmia and chlorosis, in severe paræsthesia, and in definite conditions of irritation in which they had previously used silver nitrate with success.

In ulcer the symptoms of acidity due to irritation of the glands were relieved, though the action of bismuth subnitrate was not attained.

The preparation is given in doses of half to one teaspoonful with about 100 c. c. of water, about half to one hour before the principal meals, 3 times a day. Larger doses may be used without fear of unpleasant secondary effects.

### Nitroglycerin tablets.

M. Michaelis refers to the action of nitroglycerin in an article on the treatment of angina pectoris. The effect of this remedy is displayed more slowly than in the case of amyl nitrite, but it is more prolonged. Nitroglycerin is prescribed in the form of a mixture or of tablets:

Rp. Nitroglycerin.	0.03 gramme ( $\frac{1}{2}$ grain)
Spirit. vini	10.0 grammes ( $\frac{1}{3}$ oz)
Syr. aurant.	20.0 „ ( $\frac{2}{3}$ oz)

Sig.: 20 to 30 drops to be taken several times a day.

Instead of this mixture the commercial tablets can be used with advantage in suitable doses. The tablets contain 0.6 milligramme ( $\frac{1}{100}$  grain) of nitroglycerin each. S. B.



Ward found them particularly efficacious in chronic myocarditis and in œdema of the lungs. In the latter case very large doses may be given. The author gave as much as 5 milligrammes ( $\frac{1}{12}$  grain). In a patient with myocarditis and œdema of the lungs he gave a tablet (0.0006 gramme [ $\frac{1}{100}$  grain]) every half minute for 15 minutes. He then repeated the dose at longer intervals until the danger was over, and the patient felt well. Another patient took as much as 0.2 gramme (3 grains) of nitroglycerin a day, and was always able to get over the attack by its use.

### Novaspirin.

B. Koerner admits that novaspirin has a less powerful action than aspirin, but he points out that novaspirin does not produce the same unpleasant secondary effects. In his opinion it is specially suited for the treatment of neurasthenic and tuberculous patients, for, unlike aspirin, it does not give rise to severe perspiration. He has used it for years in influenza where there is severe pain of the muscles and nerves. In these cases a very few tablets suffice to produce a satisfactory result without giving rise to buzzing in the ears or to gastric trouble. A further indication for novaspirin is afforded by slight insomnia in neurasthenia, hysteria and general nervousness, when opiates and other hypnotics are to be avoided. To produce the desired effect it is absolutely necessary to give the preparation (1 gramme [15 grains]) in a considerable quantity of warm water, and in no case should the tablets be taken dry. By this method of administering it the drug is absorbed more readily, it acts better and causes no secondary effects. In toothache due to neuralgia the author also recommends novaspirin. Even in carious teeth and actual disease of the pulp it is of good service, and may be given in doses amounting to 6 tablets a day. Novaspirin treatment is also of advantage in acute digestive disturbances of the stomach caused by fermentation, and in hyperacidity, intestinal disease and chronic diarrhœa. In these cases the following prescription is used:

Rp. Novaspirin                      0.5 gramme ( $7\frac{1}{2}$  grains)

Extract. Opii                      0.02 „ ( $\frac{1}{3}$  grain)

M. Mitte X. Sig.: One powder three times a day.

Koerner, *Therapeutische Monatshefte* 1910, No. 5.

Ward, *Albany Medical Annals* 1909, *Zentralblatt für innere Medizin* 1910, No. 34, p. 864.

E. Hartmann also found that novaspirin agreed well in most cases. He advocates its use especially when aspirin causes secondary effects. It may be used with advantage in children. Children under 12 years of age are given 0.5 gramme ( $7\frac{1}{2}$  grains) 3 to 4 times a day. Patients over 12 years 1 gramme (15 grains) 2 to 3 times a day.

### Novocain.

Overton is well known to have enunciated a theory according to which the free alkaloids when used as narcotics have a more powerful action than their salts. This theory was extended by O. Gros to the bases of the local anæsthetics. He demonstrated in animals that solutions of salts of cocaine, novocain, alypin and eucaine to which an alkali had been added showed a considerable increase in their anæsthetic properties. In practice sodium bicarbonate is recommended for this purpose. For local anæsthesia A. Læwen tested this method particularly with novocain. He found on using a solution of novocain, sodium chloride and sodium bicarbonate that the anæsthesia obtained set in earlier than is the case when novocain solution is used, while it continued for a far longer time. As the result of his trials he gives the following strengths of solutions:

	I.	II.	III.	IV.
Sod. bicarb. puriss.	0.15	0.20	0.25	0.15
Sod. chlor.	0.10	0.20	0.50	0.50
Novocain.	0.60	0.75	1.00	0.50
Aq. dest. steril.	30.00	50.00	100.00	100.00

For sacral anæsthesia the author used solutions I and II. Solution I was used for strong persons, 20 c. c. being injected extradurally. Of solution II 20 to 25 c. c. were injected. For regional anæsthesia solutions I, II and III are used. For the usual interruption of communication in the fingers, the hand and the toes, solution III is recommended. With solutions I and II the author has been able to interrupt the conduction of pain in long, large nerve roots, such as the sciatic nerve. In the extraction of teeth solution III is best used. After the injection of 2 to 5 c. c. anæsthesia is said to take place in 2 minutes.

Hartmann, Wiener medizinische Zeitung 1910, No. 9.

Gros, Münchener medizinische Wochenschrift 1910, No. 39.

Læwen, Münchener medizinische Wochenschrift 1910, No. 39.

For pure infiltration anæsthesia no special advantages are to be obtained from solutions of novocain bicarbonate.

E. Gross reports on lumbar anæsthesia with novocain in gynæcological examinations. As a rule he used 2 to 3 c. c. of a 5 p. c. solution of novocain to which a little suprarenin was added. He obtained complete anæsthesia in 87.5 p. c. of his cases, partial anæsthesia in 9 p. c. In 3.5 p. c. it failed completely. Serious secondary effects were observed in only one case among 615, when it took the form of abductor paralysis, and this passed off after about 2 months. In about 10 p. c. of the cases headache occurred. This was successfully treated in its slighter forms by antipyrine and pyramidon while the more severe headaches, which were usually localised to the back of the head, frequently continued for weeks, and resisted all treatment.

Local anæsthesia by novocain in the treatment of endometritis and abortion is described by A. Kraatz. His trials led him to the conclusion that injections of 20 c. c. of the solution obtained from 1 tablet (0.125 gramme of novocain and 0.000015 gramme of suprarenin) in 25 c. c. of normal saline solution produced sufficient loss of sensibility for dilatation, curetting and the introduction of thick laminaria tents. With regard to the sterility of the commercial tablets, K. H. Kutscher found that 4 to 8 p. c. of them contained spore-forming bacilli. It is therefore necessary to specially sterilise the solution of the tablets. The possibility of decomposing the suprarenin by doing so may be prevented by the addition of a small quantity of hydrochloric acid.

For local anæsthesia in dental practice H. Bunte and H. Moral suggest the two following solutions:

	I.	II.
Rp. Novocain.	1.50	0.50
Sod. chlor.	0.92	0.92
Thymol	0.02	0.02
Aq. dest.	ad 100.00	100.00

Solution I is for adults, solution II for children. One drop

Gross, Gynäkologische Rundschau 1910, No. 17.

Kraatz, Zentralblatt für Gynäkologie 1910, No. 22.

Kutscher, Deutsche medizinische Wochenschrift 1910, No. 24.

Bunte-Moral, Deutsche Monatsschrift für Zahnheilkunde 1910, No. 2.



of suprarenin (1:1000) should be added to each c. c. of the solution immediately before use.

### **Novoiodin.**

The antibacterial action of hexamethylenetetramine has been known for a number of years. For this reason it has been used as a preservative in the place of formaldehyde. Recently, it has been found that the iodine compound of hexamethylenetetramine has a bactericidal action which renders it suitable for the treatment of wounds. The iodine compounds of hexamethylenetetramine were first described by H. E. L. Horton. On the addition of a solution of iodine (2 molecules) in alcohol to an aqueous solution of hexamethylenetetramine, a greenish-yellow, crystalline precipitate of hexamethylenetetramine di-iodide,  $C_6H_{12}N_4J_2$ , is obtained, which is sparingly soluble in alcohol. Similarly by using 4 molecules of iodine a reddish-brown crystalline precipitate of hexamethylenetetramine tetra-iodide,  $C_6H_{12}N_4J_4$ , is obtained, a substance which dissolves in alcohol, acetone and chloroform, and may be obtained in brown crystals by recrystallisation.

Hexamethylenetetramine di-iodide is now issued commercially mixed with equal parts of powdered talc under the name of "Novoiodin". It forms a fine, light brown powder, quite free from smell, almost insoluble in all solvents; it is easily worked up with fatty oils, liquid paraffin, glycerin and collodium to form 10 to 20 p.c. suspensions.

Novoiodin is used as a non-irritant powder which causes no crusts to form, especially for the treatment of wounds. It cleanses foul wounds, abolishes the evil smell, stimulates granulation, and has a great power of absorbing discharges. It is hence specially indicated in injuries, operation wounds, abscesses, cellulitis and in gonorrhœal and syphilitic affections. For injection into cold abscesses a suspension is used of 20 grammes ( $\frac{2}{3}$  oz) of novoiodin in 100 grammes ( $3\frac{1}{3}$  oz) of sterile olive oil; for the treatment of cervical catarrh, etc., pessaries prepared with cacao butter containing 3 p.c. of novoiodin are used, and for the treatment of anal fissure suppositories each containing 0.4 gramme (6 grains) of novo-

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Horton, Berichte der deutschen chemischen Gesellschaft Berlin 1888, I, p. 2001.

iodin. For the treatment of wounds a 20 or 33 p.c. novoiodin gauze is also suitable. With regard to the efficacy of novoiodin, the publications of L. v. Zumbusch, E. L. Fieber, R. Polland, F. v. Forster, B. Gerber and R. Katholicky should be consulted.

### **Oleum Chenopodii anthelmintici.**

The use of oleum chenopodii\*) in ascariasis has been taken up recently by M. Gockel who used Brünings's method. In the doses required for the treatment of this disease the preparation may be regarded as non-poisonous. The urine assumes a lemon-yellow colour after taking the oil, and in the fæces mucus is occasionally noticed, but this is not accompanied by pain on defæcation. The author observed headache, vomiting and severe nausea, effects which may be due to the eructation following the use of the oil, and to its disagreeable taste. The oil is therefore best given in capsules, or at any rate in combination with menthol, hot milk coffee being taken with it, and the patient kept in bed for a few hours. To make quite sure of a successful result the treatment should be carried out when the stomach is empty, and repeated on two consecutive days. The treatment should be extended over two days even when worms are passed on the first day. Patients under 14 years of age are given 2 doses a day, those over 14 years 3 doses a day. On each day the patients are also given half to two teaspoonfuls of castor oil 2 hours after the last dose. In adults two teaspoonfuls of castor oil are needed, for chenopodium oil has a constipating action, and smaller doses do not produce an evacuation of the bowel. The age of the patients treated by the author ranged from 6 years upwards. The doses prescribed by him for patients of 6 to 8 years were 8 drops, for patients of 9 to 10,

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Zumbusch, Wiener klinische Wochenschrift 1910, No. 18.

Fieber, Zentralblatt für Chirurgie 1910, No. 19.

Polland, Münchener medizinische Wochenschrift 1910, No. 32.

Forster, Wiener medizinische Wochenschrift 1910, No. 30.

Gerber, Pester medizinisch-chirurgische Presse 1910, No. 33.

Katholicky, Wiener klinische Rundschau 1910, No. 46.

\*) See Merck's Reports 1906, p. 179.

Brünig, Medizinische Klinik 1906, No. 29.

Gockel, Münchener medizinische Wochenschrift 1910, No. 31.

10 drops, from 11 to 16 years, 12 drops and above 16 years 12 to 16 drops. For adults he prescribed:

Rp. Ol. Chenopod. anthelmint. m. XVI.

Menthol 0.2 gramme (3 grains)

M. Mitte VI ad capsul. gelatinos.

Sig.: Three capsules on each of two consecutive days (1 capsule every 2 hours) with hot milk-coffee, in the forenoon.

Rp. Ol. Ricin. 70.0 grammes ( $2\frac{1}{2}$  oz)

Sig.: 2 tablespoonfuls on each of two days, in beer froth, to be taken 2 hours after the third capsule.

In oxyurides chenopodium oil appears from Gockel's results to have no specially powerful action.

### **Oleum terebinthinæ.**

A communication by W. J. J. Arnold shows oil of turpentine to be valuable in the treatment of typhoid. At the beginning of the treatment the author gave the patient an enema consisting of 30 grammes (1 oz) of oil of turpentine and 600 c. c. (20 oz) of olive oil. The patient was made to lie in a position which caused the mixture to be evenly distributed throughout the large intestine. For this purpose the lower part of the bed was suitably raised. The injection is repeated the next day, and subsequently every other day until convalescence has set in. After the third injection or so the oil of turpentine should be reduced to 15 gramme ( $\frac{1}{2}$  oz) the olive oil to 450 c. c. (15 oz). If it be desired to clean out or evacuate the bowel thoroughly before commencing this treatment calomel is given in repeated small doses and a subsequent accumulation of fæces may be prevented by the administration of castor oil. With the oil injections quinine is given in an aqueous solution containing hydrochloric acid. By means of this treatment the author obtained excellent results. The abdomen was never distended, the headache left off after two days at the longest, there was never delirium, and of 30 cases only one ended fatally. Convalescence occurred in most cases after a week, at the most after 17 days.



**Olintal.**

A preparation of myrrh is issued under this name. It was recommended by Schenk for the treatment of diphtheria. He describes it as a liquid myrrh soap to which has been added 0.5 p. c. of menthol and 0.5 p. c. of camphor. It has an agreeable odour, an alkaline reaction, and it is soluble in water. The preparation may be used internally and externally. Ströll's communication on the use of tincture of myrrh in diphtheria, and the successful results of several years' treatment with it, led Schenk to try this form. Olintal is indicated in diphtheria and phthisis. Adults are given a teaspoonful 4 times a day in a glass of sugar and water, children 20 to 50 drops in sugar or in sugar and water. For inhalation and gargling half a teaspoonful is prescribed in a glass of water. In children who are not able to gargle, this solution is used as a spray. In affections of the neck the author also applies compresses to the region of the pharynx. They are soaked in half a teaspoonful of undiluted olintal.

**Orcin.**

F. Blumenthal, in testing urine for pentoses, believes that the addition of iron chloride to the reagent, as suggested formerly by Bial, is not practical, for the reagent loses its reliability by this addition. He recommends the following method of applying the test for pentoses:

3 c. c. of urine are heated to boiling after the addition of about 5 to 6 c. c. of fuming hydrochloric acid (specific gravity 1.19) and a pinch of orcin. After boiling for a short time the presence of pentose is indicated by the appearance of a bluish-green or bluish-violet colour. If this colour does not appear the urine contains no pentose. If the fluid is kept boiling a little longer the colour darkens and becomes more pronounced; boiling should then cease. If bluish-green flakes separate out there is a grave suspicion of the presence of pentose in the urine. If there is any doubt about the colour, amyl alcohol should be added

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Schenk, *Zeitschrift für innere Medizin* 1910, No. 32, p. 801.

Ströll, *Allgemeine medizinische Zentralzeitung* 1893, No. 30.

Blumenthal, *Medizinische Klinik* 1910, No. 14, p. 550.

Bial, *Merck's Reports* 1903, p. 140.

to the mixture, as it takes up the colour. The amyl alcohol solution shows the characteristic absorption bands between C and D. The greenish-blue colour, or the greenish-blue precipitate is proof of the presence of pentose, and no error is possible unless the urine to be tested contains an abnormally large amount of glycuronic acid as the result of taking certain drugs. The only question is whether a bluish-violet colour of the amyl alcohol proves the presence of pentose; in such cases the osazone must be prepared, and its melting point determined (155—160° C.). For further details the original paper must be consulted.

### Organotherapeutic Preparations.\*)

#### Corpora lutea.

The physiological properties of the corpus luteum have been dealt with in various interesting papers. Special mention may be made of the communications of J. Miller, L. Loeb and N.A. Bielow. Miller doubts the existence of an internal secretion of the corpus luteum, but Bielow believes that the secretion from the organ lowers blood pressure and diminishes the pulse-rate, and is of great importance in all respects to the female organism. From its power of lowering the blood pressure the secretion of the corpus luteum is to be regarded as antagonistic to the secretion of the suprarenals. A more detailed account of the extensive works that have appeared on this subject cannot be given here.

E. MacDonald has made a therapeutic trial of extract of corpora lutea. He regards it as an established fact that pregnancy may be checked by interference with the

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\*) The accounts given here of the organotherapeutic preparations complete the series of articles on "Organotherapy and Organotherapeutic Preparations" in my Annual Reports for 1908.

Miller, Münchener medizinische Wochenschrift 1910, No. 10, p. 553. — Deutsche medizinische Wochenschrift 1910, No. 17, p. 821.

Loeb, Zentralblatt für Physiologie 1909, Medical Record 1910, 25<sup>th</sup> June. — Klinisch-therapeutische Wochenschrift 1910, No. 35, p. 851. — Deutsche Medizinal-Zeitung 1910, No. 10, p. 170.

Bielow, Russkij Wratsch 1910, No. 12.

MacDonald, Journal of the American Medical Association 1910, 16<sup>th</sup> July.

corpus luteum in the early stage, before the ovum has become embedded in it, while the internal secretion of the corpus luteum has an effect on menstruation which justifies the use of this organic preparation in premature menopause and in scanty menstruation. In such cases he prescribed 0.3 gramme (5 grains) of dry extract of corpus luteum 3 times a day, and obtained a favourable result in 7 cases out of ten. He obtained no effect in older cases; therefore the administration of the organic preparation should be commenced as early as possible. Less encouraging results were obtained in surgical menopause, only one case in ten showing a definite effect. The author believes that this organic preparation may be of good service after operations, when it may prevent the occurrence of abortion; he points out that ovarian substance cannot be substituted for corpora lutea for this purpose.

#### **Glandulæ parathyroideæ (Parathyroidin).**

Based on two cases of thyroidectomy, E. Bircher explains the great difficulty of performing these operations with the least disturbance to the parathyroids, and he describes the therapeutic use of dried parathyroid in the treatment of post-operative tetany due to removal of the parathyroids. The parathyroids are so variable in their size and position that the most skilful operator may be unable to avoid their partial removal when operating upon the thyroid gland. Hence great interest attaches to two cases in which tetany, appearing after the operation, was rapidly cured by parathyroid gland tablets. The author was not able to influence the tetany by thyroid gland; with parathyroid gland, however, he rapidly obtained a successful result. This confirms the statement of Vassale, Mannescu, Loebenthal and Wiebrecht that tetania parathyreopriva may be successfully treated by dried parathyroid gland. The administration of parathyroid tablets should be adjusted in accordance with the symptoms of tetany. Three tablets may be given 3 to 4 times a day, until the symptoms subside, when they may be discontinued; or when the symptoms appear a large dose may be given, and its action awaited before giving more. The final result was obtained in the cases described



by the author after an intermittent treatment lasting 7 or 10 days.

Another indication for the use of parathyroid is afforded by the pharmacological experiments of Canal. He found that the secretions of the parathyroid glands prevented the organism from becoming impoverished in lime, and regulated the calcium metabolism. In animal experiments he was able to show that the removal of the parathyroid glands led to interference with the consolidation of bones after fractures; cartilaginous union occurred, but no lime was deposited. Whether the use of parathyroidin will be of value in delayed consolidation of fractures must be ascertained by suitable trials.

### **Glandulæ salivales.**

The investigations of G. Pagliai show that the salivary glands yield an internal secretion, the importance of which to the organism should not be undervalued. This view was first expressed by Zagari and Baccarani; to prove it the author experimented on rabbits, extirpating the whole of their salivary glands. All the animals died of cachexia in the course of about 3 weeks. Animals that received injections of extract of salivary gland immediately after the removal of their glands, and those in which fresh glands were implanted, remained well. The treatment with this organic preparation showed a good effect even when the injections were delayed until cachexia had actually set in. Whether the glandulæ salivales, in the form of an extract or a powder, will prove of therapeutic use in cachexia must be determined by further trials. As far as I know there is not, as yet, a suitable preparation on the market.

### **Glandulæ thymi.**

The physiology and pathology of the thymus has been described by C. Hart and O. Nordmann, and by Klose and Vogt, based on their experimental work. Their results are of some importance to organotherapy; Hart and Nordmann found the thymus to be an important, possibly indispensable

Canal, *Gazzetta degli ospedali e delle cliniche* 1909, No. 93.

Pagliai, *Rivista critica di clinica medica* 1910, No. 26.

Hart-Nordmann, *Berliner klinische Wochenschrift* 1910, No. 18, p. 814.

organ during the period of growth of the organism. Its action is in relation to the assimilation of food and to the regulating action of the cardiac arteries, it probably determines the power of the organism of resisting bacterial influences. The development of the lymphatic glands is also dependent on the thymus. The total (but not the partial) extirpation lead to symptoms characterised by a gradual loss of vital power. An excess of thymus, or of the products of its metabolism, causes toxic symptoms which subside rapidly when the excess is removed.

Klose regards the thymus as the organ principally concerned in the synthesis of nuclein. Its removal leads to an increase in the circulation of the blood of less complex compounds (phosphoric acid?) These modify the calcium metabolism in such a way as to dissolve lime, or to keep it in solution; hence the organism is impoverished in lime, and fractures refuse to unite, or unite tardily. The chief organ to take the place of the thymus is, very probably, the spleen. Experiments on 54 dogs showed that complete removal of the thymus led to no notable changes in the animals in the first months. For several months there is an increased desire for food, and the animals grow fat; they then lose weight in the course of 4 to 14 months, and idiotia thymica sets in, the animals become cachectic, and their bones soften and become liable to spontaneous fracture. Finally all the animals die.

#### **Glandulæ thyroideæ (Thyroidin).**

In a paper by E. P. Pick and F. Pineles experimental proof is adduced to prove that iodothyrene is not the only active constituent of the thyroid gland, and that in fact it is not even an active substance of the thyroid. The authors found that myxœdematous goats, when given pigs' thyroid gland and thyroglobulin, lost their symptoms in a striking manner. In a lesser degree the same effect was obtained with secondary albumoses obtained by digesting thyroid glands for 2 days with pepsin hydrochloride. No effect was obtained, however, by feeding with iodothyrene,

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Klose-Vogt, Münchener medizinische Wochenschrift 1910, No. 16, p. 874.

Pick - Pineles, Zeitschrift für experimentelle Pathologie und Therapie Vol. 7, No. 2, p. 518.

with primary albumoses obtained by 2 days' pepsin hydrochloride digestion, or with the products of long continued pepsin and trypsin digestion. Hence the active substance of the thyroid gland is destroyed by splitting up the albumin of the thyroid gland, in a process such as leads to the formation of iodothyrene. Reid, Hunt and Seidell adhere to the well known view that the iodine determines the action of the thyroid gland. They found that the poisonous action of acetonitrile could be considerably diminished in certain animals by thyroid gland substance, and that the diminution was proportional to the amount of iodine contained in the thyroid gland used. The authors must admit, however, that this action takes place to some extent with thyroid gland preparations that contain no iodine.

From the therapeutic point of view the most important recent communication on thyroïdin treatment is that of A. Siegmund. He showed that the vomiting of pregnancy could be cured by thyroïdin. In treating hyperemesis with this preparation several points need to be considered. The rules regulating the times for giving the drug have been laid down by W. Fliess. Just as quinine is given some hours before the rise of temperature, so thyroïdin must be given a few hours before the vomiting is at its worst, and it must be given on an empty stomach. Hence it is given at 5.30 or 5 a. m., in bed, and if necessary the patient must be wakened for the purpose. She then sleeps for a few hours more, and takes her breakfast in bed. The treatment is repeated at 9 o'clock, and again half an hour before lunch and supper, and before going to bed. The morning dose should be large, not less than 0.3 gramme (5 grains), and 0.45 to 0.6 gramme (7—9 grains) may be given. Should vomiting occur at any other time than in the early morning, an additional full dose of thyroïdin must be given a few hours before. Hence the time of administration and the amount to be given must be subject to medical supervision. A point to note is that larger doses are usually required at the beginning of the treatment, for at this time there are

Hunt-Seidell, Arbeiten aus dem Gesundheitsamt der Vereinigten Staaten von Nord-Amerika, Washington 1909, Klinisch-therapeutische Wochenschrift 1910, No. 23, p. 363.

Siegmund, Zentralblatt für Gynäkologie 1910, No. 42.

Fliess, Der Ablauf des Lebens, 1906, Wien, Published by F. Deuticke.



more toxic substances present in the blood which require to be rendered innocuous. The thyroidin treatment is considered by Siegmund to be free from danger.

Further proof of the value and efficacy of thyroidin in endemic cretinism has been furnished by A. Eysselt von Klimpély. He finds it important to commence treatment with the organic preparation as early as possible, although good results may be obtained even in fairly old patients. By giving 0.3 to 0.45 gramme (5—7 grains) of thyroidin daily, the author obtained very satisfactory, occasionally surprising results. In almost all cases he observed a growth in height, even in a patient of 22. Further, the growth of the base of the skull led to an improvement in the physiognomy, a better temper, with sexual and dental development. If the treatment be begun in early childhood, severe disturbances of speech and hearing may be greatly benefited. There is no important disadvantage in thyroidin treatment. At the most, transitory disturbances may occur, such as vomiting or tremors of the fingers. The loss of weight which may occur during the treatment is of no disadvantage to the cretin, for it is easily made up again by suitable feeding. The wasting is merely due to loss of fat resulting from increased oxidation; there is no loss of nitrogen worth mentioning. Hence thyroidin treatment is safe even in the treatment of obesity. In feeble persons with degenerate cardiac muscles constant medical supervision is necessary to prevent thyroidism. K. E. Wagner treated 149 patients, giving them 0.12 gramme (2 grains) of *glandulæ thyroideæ* twice a day, and obtained excellent results. The weight fell by rather more than half a pound a day. In 17 cases only was it necessary to interrupt the treatment for a time because of lassitude, nervous excitement and an accelerated pulse. A. Lorand also obtained good results with the use of thyroid gland in obesity. In his experience the treatment is best tolerated in conjunction with alkaline waters. In severe cases 4 or more tablets may be given daily for weeks; and thyroidin may be replaced at intervals

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Eysselt von Klimpély, *Wiener medizinische Wochenschrift* 1910, No. 7—14. See also E. Bircher, *Archiv für klinische Chirurgie* Vol. 91, No. 3.

Wagner, *Wiener klinische Wochenschrift* 1910, No. 11.

Lorand, *Wiener medizinische Wochenschrift* 1910, No. 14 and 15

of a few days by small doses of alkaline iodides. In youthful adiposity, especially in girls approaching puberty, H. Stern avoids secondary effects from thyroïdin by prescribing it with arsenic and adonidine as follows:

Rp. Sod. cacodyl.	0.0005 gramme ( $\frac{1}{120}$ grain)
Adonidin.	0.002 „ ( $\frac{1}{32}$ „ )
Gland. thyr. sicc. pulv.	0.05 „ ( $\frac{3}{4}$ „ )

M. Ft. tabl. Mitte 50. Sig.: 3 to 4 tablets a day.

Thyroïdin treatment was also found useful by L. Levi and H. de Rothschild in asthmatic conditions, by Ph. Levison in dementia præcox, by Comby in enuresis, and by E. Roques in scleroderma.

### Hypophysis cerebri.

In a comprehensive experimental study of the function and the pharmacological action of the hypophysis, G. Franchini confirms the results of Cerletti and Sandri, who found that extract of hypophysis might produce serious disturbances of metabolism. He found that it caused a loss of calcium and magnesium salts; hence it seems to contain a very active substance, even in small doses, just as in the case of the suprarenal. In addition to its general toxic action on rabbits and guinea-pigs, it has a special action on the intestinal canal, leading to ulceration and hæmorrhage. This action is specially evident on intravenous use; less on subcutaneous and internal administration. The anterior lobe, separated from its epithelial layer, merely produces slight disturbance in rabbits, even in large doses, though with its epithelial layer its action may be fatal. The isolated posterior lobe has a special influence on metabolism, and on the organs and vessels of the abdomen and pelvis. It contains a substance which produces definite my-

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Stern, Berliner klinische Wochenschrift 1910, No. 30.

Levi-Rothschild, Gazette des hôpitaux 1910, No. 58, p. 846.

Levison, Hospitalstidende 1909, p. 1116.

Comby, Klinisch-therapeutische Wochenschrift 1910, No. 36, p. 884.

Roques, Annales de dermatologie et de syphiligraphie 1910, No. 7.

Franchini, Berliner klinische Wochenschrift 1910, No. 14, 15 and 16.

Cerletti, Atti della reale academia dei lincei 1906, 26th April and 1908, 3rd May.

Sandri, Rivista di patologia nervale e mentale 1908, p. 518.

driasis in a frog's eye, though it does not give the other reactions of adrenalin.

G. G. Wray was no doubt acting on these facts in using intravenous injections of extract of hypophysis for the treatment of surgical shock in place of adrenalin, the action of which in severe collapse is said to be limited to an effect on the hypotension. He obtained satisfactory results. He found extract of hypophysis to act, not only on the blood vessels but also on the heart, causing transitory diuresis. It also causes uterine contractions, according to a communication by J. A. Henton White. He reports a case of a woman of 28 with pneumonia, suffering from atony of the uterus after lumbar anæsthesia and delivery. After the injection of 12 drops of extract of hypophysis a powerful contraction of the uterus took place, the hæmorrhage ceased and the pulse improved. W. Blair Bell found the action of extract of hypophysis in atony of the uterus better than that of ergotin. L. Williams recommends it for the treatment of tuberculosis, for it raises the blood pressure, and increases the appetite; also for the treatment of weak heart, and particularly in surgical shock. A success is also reported with the use of extract of hypophysis in the treatment of Graves's disease and paralysis agitans. For subcutaneous use the author gives 0.1 to 0.3 gramme ( $1\frac{1}{2}$  to 5 grains) of the extract for a dose. P. Thaon considers that extract of hypophysis should only be used in persons whose kidneys are perfectly healthy, for in sheep, after the injection of a dose amounting to an entire gland, he observed hæmaturia, wasting and death. At the pathological examination of these animals, the kidneys showed subacute glomerular nephritis with severe congestion.

L. v. Frankl-Hochwart and A. Fröhlich tested hypophysin (pituirine), an extract of hypophysis of constant composition, for its pharmacological action on the sympathetic

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Wray, *Klinisch-therapeutische Wochenschrift* 1910, No. 6, p. 167.

White, *British Medical Journal* 1910, 28<sup>th</sup> May, p. 1282.

Bell, *British Medical Journal* 1909, 4<sup>th</sup> December. — *Nouveaux remèdes* 1910, p. 318.

Williams, *Münchener medizinische Wochenschrift* 1910, p. 1262.

Thaon, *Tribune médicale* 1910, No. 45.

Frankl-Hochwart und Fröhlich, *Archiv für experimentelle Pathologie und Pharmakologie* 1910, Vol. 63, p. 347.



and autonomous nervous system; they found that the preparation produced uterine contractions and stimulated the muscles of the bladder, so that it would be desirable to test it therapeutically in suitable cases.

### **Lentocalin.**

Recent communications by R ö m e r show that the treatment of senile cataract with an organic preparation is less promising than was formerly supposed\*). The author considers that the acuity of vision had not been accurately measured in the earlier examinations. Moreover spontaneous improvement in the acuity of vision is apt to occur, especially in subcapsular senile cataract, so that he does not consider that much improvement in the acuity of vision is to be expected from treatment with lens substance. The opacity of the lens does not yield to the treatment; hence the value of lentocalin must, at best, be limited to checking the advance of early subcapsular cataract. It is still quite undecided whether the advance can actually be checked. The author considers it advisable to settle the point by further trials.

### **Lien.**

A practical method of dealing with hæmophilic hæmorrhage is suggested by L. Plumier. It consists in the combined use of extract of spleen and peptone. The peptone is injected as a 5 p.c. sterile solution, subcutaneously or into the serous cavities, the usual dose being 10 c.c. The injection must be made slowly, for otherwise the blood becomes less coagulable than ever, and the desired effect is not obtained. The extract of spleen is applied locally, tampons of wool being soaked in it and placed on the affected spot, as for instance in the bleeding cavity after the extraction of a tooth. Its action is said to be better than that of the blood serum commonly used for this purpose.

### **Medulla ossium.**

D a l m a y e and M e z i g state that in internal infective diseases (malaria, typhoid fever, etc.) there is always a

Römer, Medizinische Klinik 1910, No. 37, p. 1465.

\*) See Merck's Reports 1909, p. 250.

Plumier, Scalpel 1910, 19<sup>th</sup> June.

Damaye-Mezig, Bulletin général de thérapeutique 1910, No. 24.

stage up to which it is possible to neutralise the injurious effects of the poisons circulating in the organism, and to produce active phagocytosis. For this purpose raw spleen and raw bone marrow are said to be specially well suited. If this form of organotherapy is to be of use it should be commenced as soon as possible. The authors have given spleen and bone marrow chopped up in honey or in stewed fruit, and have obtained good results.

### **Ovaria.**

Wittgenstein observed that ovarian extract affects the virulence of tubercle bacilli so that they are only able to produce chronic tuberculosis in animals. The animals infected with these bacilli live longer than those infected with emulsions of bacilli of equal strength but not treated with ovarian substance. In recognition of this fact, ovarian treatment acquires interest in the treatment of human tuberculosis.

Theoretical explanations regarding the internal secretion of the ovaries in relation to other organs is given by L. v. Lingen. The results cannot be given in abstract and the original paper is very well worth reading.

### **Pancreas hormone.**

A hormone corresponding to peristaltic hormone\*) was first prepared by Zuelzer from the pancreas of dogs and horses. The therapeutic investigation of this pancreas hormone has been carried out by J. Forschbach. So far it has led to no satisfactory result. In a case of diabetes mellitus and one of diabetes insipidus the intravenous application of the remedy in man was found by the author to cause a rise of temperature and a number of other symptoms pointing to a severe toxæmia. Shortly after the injection the patients exhibited a disquieting degree of pros-

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Wittgenstein, Wiener klinische Wochenschrift 1909, No. 51.  
von Lingen, Petersburger medizinische Wochenschrift 1909, No. 50.

\*) See the next article.

Zuelzer, Deutsche medizinische Wochenschrift 1908, No. 32. —  
Zeitschrift für experimentelle Pathologie und Therapie 1909,  
Vol. 5, p. 307.

Forschbach, Deutsche medizinische Wochenschrift 1909, No. 47.  
— Deutsche Medizinalzeitung 1910, No. 27, p. 474.

tration; the pulse was rapid, and vomiting set in. In the patient with diabetes insipidus, there appeared on the following day not only stomatitis, but severe herpes labialis which took 8 days to heal. The trials of Zuelzer and Forschbach go to show that the intravenous injection of pancreas hormone leads to a diminution in the excretion of sugar, but the preparation is clearly unfit for general use, even the method of obtaining it being as yet crude. We require a preparation that is free from objection, and this will probably follow from a different method of preparation.

### **Peristaltic hormone (Hormonal).**

Some time ago G. Zuelzer, in common with M. Dohrn and A. Marxer, showed that in the cells of the gastric mucous membrane a hormone is formed\*) which has a specific effect on intestinal peristalsis. To make a peristaltic hormone of use for treatment we must have a preparation that can be introduced straight into the blood stream without danger. Hence, even though the hormone might be extracted from the gastric mucous membrane of animals, Zuelzer fears that pathogenic bacteria, such as the tetanus bacillus, might get into the preparation. For this reason he prepared peristaltic hormone from the spleen, which his experiments showed to contain a relatively very large amount of hormone. The spleen is thought by the author to be, not the place of formation of this hormone, but its place of storage. It is possible to obtain from the spleen a sterile preparation.

The principal indication for the use of peristaltic hormone is chronic constipation. Zuelzer selected the intravenous method as the best; it caused no more than a slight rise of temperature (hormone fever), and slight local pain, while it did no injury to the heart in any case. Of the persons

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Zuelzer-Dohrn-Marxer, Berliner klinische Wochenschrift 1908, No. 46.

Zuelzer, Medizinische Klinik 1910, No. 11.

\*) Hormones are chemical products of metabolism formed in the various organs of the animal body, and carried by the circulation to remote organs where they show a specific activity. Unlike the nutritive substances, they are stimulating bodies which excite certain groups of cells to perform particular functions (Starling, Zentralblatt für die gesamte Physiologie und Pathologie des Stoffwechsels 1907, No. 5 and 6).



in whom the hormone was injected he obtained a cure in 71 p. c. of the cases, and no result in 29 p. c. In the cases cured defæcation became normal, and has continued, so that one or two spontaneous copious motions are obtained daily without the use of any purgative. The action of the injections set in on the second or third day; occasionally not till the fifth or seventh day. The duration of the cure has already been observed to extend to half a year.

Another indication is furnished by intestinal paralysis following operations, or due to colic. In some of these cases while the secondary effects were slight the author has observed very favourable results, so that the further trial of the new preparation is to be recommended. Zuelzer points out that the intravenous injection of peristaltic hormone is a harmless procedure, the effect of which is so far from being a violent one that there is no fear of serious disturbance even in organic obstruction. The dose of the hormone is 15 to 20 c. c. Henle used peristaltic hormone in a number of cases of post-operative paresis, some of them severe cases; he attributes the successful result to the action of the preparation, though in particular cases this may be difficult to demonstrate directly. As a rule the treatment was followed, after 6 to 8 hours, by the passage of flatus either spontaneously or after intestinal irrigation in a way that could not be obtained without the hormone.

The cases of constipation that are best suited for the hormone treatment are thought by Saar to be unknown as yet. At any rate the remedy does not always act, as shown by a case described. Saar recommends that the injections be given in the morning, to enable the febrile reaction to pass off during the day.

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### Ovogal.

The same results as those previously obtained by Wörner have been obtained by Eichler and Latz in animal experiments with ovogal\*). After the administration of ovogal

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Henle, Zentralblatt für Chirurgie 1910, No. 42.

Saar, Medizinische Klinik 1910, No. 11.

\*) See Merck's Reports 1906, 1907 and 1909.

Eichler-Latz, Boas Archiv für Verdauungskrankheiten Vol. XV, No. 5. — Therapie der Gegenwart 1910, No. 4.

they were able to observe a definite increase in the flow of liquid bile, and an increase in the sodium taurocholate content. Eichler lays special stress on the latter, for bile that is rich in choleic acid salts is a good solvent for cholesterin. The fear of producing hæmolysis by giving bile is said by the author to be unjustified, provided the dosage is suitable. The chief indications are acute and chronic catarrh of the liver and the bile ducts, and cholelithiasis. The preparation is best given in gelatin capsules, 0.5 gramme ( $7\frac{1}{2}$  grains) 3 to 4 times a day, until 100 capsules containing 0.5 gramme ( $7\frac{1}{2}$  grains) each have been given. This treatment is repeated after a few months, and again later. To obtain in addition a slight antiseptic action on the bile, sodium salicylate, saliformine or hexamethylenetetramine may be added from time to time. Moreover all approved dietetic, hydropathic and hygienic measures must be observed, while in suitable cases the patient must take waters as well.

### **Pantopon (Omnopon).**

The pharmacological investigations of Rose Wertheimer-Raffalovich show that pantopon\*) has a decided hypnotic action on animals, and affects the respiratory centre less than morphine. The same result was obtained by A. Loewy and W. Bergien. The latter showed further that the preparation had no effect upon the circulation. These characteristics mark out pantopon as a suitable substitute for morphine in scopolamine-morphine anæsthesia, and G. Brüstlein has suggested its use for this purpose. He directs that a syringe-ful of a 2 p.c. solution of pantopon be injected  $1\frac{1}{4}$  to  $1\frac{1}{2}$  hours before the operation, and that about half an hour later the same dose be injected subcutaneously with 0.0007 gramme ( $\frac{1}{90}$  grain) of scopolamine hydrobromide. In women an injection of 0.04 gramme ( $\frac{2}{3}$  grain) of pantopon and 0.0004 gramme ( $\frac{1}{160}$  grain) of scopolamine will suffice as a rule. The author states that

Wertheimer-Raffalovich, Deutsche medizinische Wochenschrift 1910, No. 37.

\*) See Merck's Reports 1908 and 1909.

Loewy, Münchener medizinische Wochenschrift 1910, No. 46.

Bergien, Münchener medizinische Wochenschrift 1910, No. 46.

Brüstlein, Korrespondenzblatt für Schweizer Ärzte 1910, No. 26.

this method produces a better anæsthesia than scopolamine-morphine injections. Gräfenberg thinks that the scopolamine may be omitted. He tried general anæsthesia by means of ether with pantopon injections alone, and has already obtained very satisfactory results. 1 c.c. (17 min.) of a 2 p.c. solution of pantopon is injected an hour and a half, and again half an hour before the operation; by this means deep anæsthesia may be obtained with ether in a third of the time required after morphine-scopolamine. In labour pains, pantopon is said to be of good service. In multiparæ, where labour runs a short course, a single injection is usually completely effective, while in primiparæ 2 injections of 0.02 gramme ( $\frac{1}{3}$  grain) of pantopon each, at intervals of about 3 hours, control the severe pain. The author observed no effect upon the duration of labour as a result of this treatment in consequence of the diminution of the pains. During the expulsion stage the injections should be avoided.

C. A. Ewald found pantopon to possess a curative action in diarrhœa in addition to its analgesic action. With 0.01 gramme ( $\frac{1}{6}$  grain) the author was able to produce a transitory good result in tuberculous diarrhœa. For the relief of pain pantopon is usually given internally in doses of 0.01 to 0.02 gramme ( $\frac{1}{6}$ — $\frac{1}{3}$  grain), and subcutaneously in doses of 0.02 gramme ( $\frac{1}{3}$  grain). A favourable opinion of the preparation has been reported in papers by Pertik, F. Heimann, J. Hallervorden, H. Sahli, Rodari, Rodolico and H. Haymann. The most interesting are the results of Haymann, who tried the remedy in psychiatric practice. Its value was found by the author to depend on its rapid action on subcutaneous application, so that it may be used in the case of struggling patients. Its chief

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Gräfenberg, Deutsche medizinische Wochenschrift 1910, No. 34 and 39.

Ewald, Berliner klinische Wochenschrift 1910, No. 35.

Pertik, Deutsche medizinische Wochenschrift 1910, No. 36.

Heimann, Münchener medizinische Wochenschrift 1910, No. 7.

Hallervorden, Therapie der Gegenwart 1910, No. 5.

Sahli, Münchener medizinische Wochenschrift 1910, No. 25.

Rodari, Klinisch-therapeutische Wochenschrift 1910, No. 26.

Rodolico, Giornale internazionale delle scienze mediche 1910, Vol. 32.

Haymann, Münchener medizinische Wochenschrift 1910, No. 43.



action is not so much hypnotic as sedative, and this is best shown in dealing with cases of fear and excitation. The secondary effects are not serious, and in many cases they are absent.

### Para-Monochlorphenol.

A few years ago Herrenknecht recommended a combination of para-monochlorphenol and camphor for dental practice:

Rp. Para-monochlorphenol	10.0 grammes ( $\frac{1}{3}$ oz)
Camphor. trit.	20.0 „ ( $\frac{2}{3}$ oz)
Alcohol. absolut.	3.0 „ (60 min.)

The sedative and disinfectant action of this mixture was confirmed by Cavalie, who used the following pastes with good effect for the treatment of dental caries. He prescribed:

Rp. Para-monochlorphenol	3.0 grammes (45 grains)
Menthol.	1.0 gramme (15 grains)
Camphor.	0.5 gramme ( $7\frac{1}{2}$ grains)
Eugenol.	5.0 grammes (80 min.)
Zinc. oxid. q. s. ut fiat pasta.	

Rp. Para-monochlorphenol	4.0 grammes (60 grains)
Acid. phosphor.	2 c. c. (34 min.)
Camphor.	0.5 gramme ( $7\frac{1}{2}$ grains)
Vanillin.	2.0 grammes (30 grains)
Zinc. oxid. q. s. ut fiat pasta.	

G. Blessing paid special attention to the combination suggested by Herrenknecht, and obtained very good results with it. He modified the directions for para-monochlorphenol-camphor by mixing para-monochlorphenol and camphor in the proportion of 1:2 and adding no alcohol. The action of this remedy in many cases of severe pain after the extraction of teeth for periodontitis was surprisingly good. The author placed a pledget of wool soaked in the mixture into the cavity, and closed it with wool.

Para-monochlorphenol-camphor is of good service as a disinfectant in crowning cavities, in the treatment of wounds, and in pyorrhoea alveolaris. In the last named disease Blessing carried out special trials which show that the mixture kills

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Herrenknecht, Zahnärztliche Rundschau 1907, No. 44.

Cavalie, Revue trimestrielle suisse d'Odontologie 1909, No. 3.

Blessing, Deutsche Zahnärztliche Wochenschrift 1910, No. 44.

pyorrhoeal pus bacilli in a very short time. For this reason the author regards para-monochlorophenol-camphor as superior to any previously known disinfectant and curative agent.

### **Pergenol.**

Pergenol is a mixture of sodium perborate and sodium bitartrate; when dissolved in water it is decomposed with formation of sodium tartrate and boric acid, while hydrogen peroxide is liberated. To prepare a 1 p.c. solution of hydrogen peroxide M. Lewitt uses 10 grammes ( $\frac{1}{3}$  oz) of pergenol and 120 grammes (4 oz) of water. The disinfectant action of hydrogen peroxide is well known; that of pergenol in aqueous solution has been confirmed by Croner and Schmidt. The preparation is issued as a powder and in tablets, each of which contains 0.5 or 0.1 gramme ( $7\frac{1}{2}$  or  $1\frac{1}{2}$  grains) of pergenol.

The use of pergenol in the treatment of wounds is described by R. Meyer, Sachs and Sander. The preparation is used in aqueous solution in the same way as hydrogen peroxide for washing out wounds, tooth cavities, fistulæ, etc., and for cleansing instruments. As a powder, mixed with 3 parts of talc, it may be dusted upon wounds. As a disinfectant for the mouth pergenol has been found useful by Prochnow, Golopp and Dietrich. For this purpose it may be used in aqueous solution or in tablets. The latter are also of use in laryngological and rhinological practice. For gargling, the 0.1 gramme ( $1\frac{1}{2}$  grains) pergenol tablets are recommended. Specially good results were obtained with them in children by Gotthilf, Spitzer and Meyer, for gargling is difficult to most children.

The use of pergenol in dermatology has been dealt

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- Lewitt, Allgemeine medizinische Zentralzeitung 1910, No. 40.  
Croner, Zeitschrift für Hygiene und Infektionskrankheiten 1909.  
Schmidt, Zentralblatt für Bakteriologie, Vol. 55, No. 4, p. 327.  
Meyer, Therapie der Gegenwart 1910, No. 4.  
Sachs, Deutsche medizinische Wochenschrift 1910, No. 3.  
Sander, Deutsche Zahnärztliche Wochenschrift 1909, No. 51.  
Prochnow, Deutsche Zahnärztliche Wochenschrift 1909, No. 43.  
Golopp, Berliner Zahnärztliche Halbmonatschrift 1909, No. 22.  
Dietrich, Zahnärztliche Rundschau 1909, No. 47.  
Gotthilf, Medizinische Klinik 1910, No. 8.  
Spitzer, Deutsche Ärztezeitung 1910, No. 17.

with by P. Richter and M. Lewitt. Richter used a solution of 25 grammes ( $\frac{5}{6}$  oz) of pergenol in 100 grammes ( $3\frac{1}{3}$  oz) of water to cleanse soft sores, incised boils, ulcers of the leg, open buboes, etc.; no irritant effects were produced, with the exception of a slight burning pain now and then, although pergenol solution contains a considerable amount of salts. The only disadvantage of the preparation lies, in his opinion, in the fact that it is hygroscopic. Beyer and Schmidt object to the large mass of borate needed for the solution of pergenol. In Beyer's judgment the presence of a large percentage of sodium tartrate in the solution is not immaterial when it is used for the care of the mouth. The author must be given right in this respect, for dentists lay special stress on the freedom of hydrogen peroxide from salts and acids, and object to the least trace of acid. Now that it is possible to obtain preparations which answer these requirements, it is suggested that a large percentage of salts does no harm whatever to the mouth and teeth. In conclusion mention may be made of the works of Lewinski, Greve, Ebermann, Buob, Fuchs, Neumann and Daxenberger.

### Perhydrol\*).

In a paper on the bactericidal action of certain preparations of hydrogen peroxide, Schmidt has shown that the action of perhydrol increases considerably as the temperature is raised. He therefore recommends the use of solutions warmed to 35° C. for the treatment of wounds and for the care of the mouth. In the hygiene of the mouth and teeth we have further to consider the papers

- Richter, Deutsche medizinische Wochenschrift 1910, No. 47.  
Beyer, Ärztliche Vierteljahresrundschau (Bonn) 1910, No. 2.  
Lewinski, Zahnärztliche Rundschau 1910, No. 30.  
Greve, Zahnärztliche Rundschau 1910, No. 32.  
Ebermann, Deutsche Zahnärztliche Wochenschrift 1909, No. 51.  
Buob, Zahntechnische Rundschau 1910, No. 5.  
Fuchs, Odontologische Nachrichten 1910, No. 19.  
Neumann, Archiv für Zahnheilkunde 1910, No. 4.  
Daxenberger, Wochenschrift für Therapie und Hygiene des Auges 1910, No. 14.

\*) See Merck's Reports 1900—1909, also Magnesium-Perhydrol and Zinc-Perhydrol in these Reports.

Schmidt, Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten 1910, Vol. 55, No. 4, p. 327.



of M. Holst, E. Spitzer, J. Zilz, J. Boberg, Dürr, Fischer, G. Kukay and W. Zielinsky.

To cleanse pyorrhœal pockets Boberg directs that all tartar be first carefully removed by suitable instruments; perhydrol is then introduced into the pockets by means of a horse-hair brush stiffened with soft wax; this is soaked in perhydrol and introduced into the pockets with a rotatory movement. Before re-inserting it, it must be washed every time. After the first treatment the pockets are filled with pus; this is removed by syringing with water. The pus diminishes with each application of perhydrol. After the application of the latter the gums are firmly massaged with the tips of the fingers from the roots to the crowns. This massage is repeated every day, and in addition a tooth brush is used without tooth powder. In the first stage of the disease this method gives promise of success and many teeth may be saved.

A method of treating empyema of the antrum of Highmore is described by Holst. The chief object of treatment is the removal of the pus to prevent the spread of the trouble, and this object would be achieved by washing out the antrum with normal saline solution. Unfortunately this treatment would not remove the pus from the folds and pockets of the antrum. The action of perhydrol, however, is excellent; on contact with diseased or dead organic tissues, especially pus, it effervesces vigorously, expelling the dead tissues from all recesses of the mucous membrane, while it does no harm to the healthy tissues. The antrum is cleaned out as follows: From the alveoli the antrum is first syringed out with a lukewarm, 2 p. c. boric acid solution, until the greater part of its muco-purulent contents has been removed. A syringe is then filled with about 10 c. c. of a mixture of 10 parts of perhydrol and 90 parts of water, or 17 parts of perhydrol and 83 of water (making a 3 p. c.

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Holst, *Tandlaegetidende* 1909, No. 2, p. 67.

Spitzer, *Deutsche Ärzte-Zeitung* 1910, No. 17, p. 387.

Zilz, *Österreich-ungarische Vierteljahresschrift für Zahnheilkunde* 1910, No. 3.

Boberg, *Deutsche zahnärztliche Zeitung* 1910, No. 41.

Dürr, *Deutsche Monatsschrift für Zahnheilkunde* 1910, No. 9.

Fischer, *Deutsche zahnärztliche Wochenschrift* 1910, No. 51.

Kukay, *Deutsche zahnärztliche Zeitung* 1910, No. 47.

Zielinsky, *Deutsche Monatsschrift für Zahnheilkunde* 1910, No. 9.

and a 5 p. c. solution of hydrogen peroxide), and is emptied into the antrum. A rise of pressure occurs in the maxilla, the degree of which depends on the quantity of mucus still present in the antrum. A syringe should be at hand containing water that has been boiled and then allowed to cool, and in case the pressure rises higher than the patient can bear this water is injected into the antrum without delay. At each application the perhydrol should be allowed to act on the antrum for several minutes, if the tension permits; the antrum should then be washed out several times with weak, lukewarm salt and water.

Spitzer alludes to the value of perhydrol, or of hydrogen peroxide, in the care of the mouth, especially in stomatitis, tonsillitis, scurvy etc.; a 1 to 3 p. c. solution is used. Zilz recommends it as a mouth wash to prevent stomatitis, especially in persons who wear plates. Dürr, Kukay, Fischer and Zielinsky recommend it to bleach the teeth. Dürr points out specially that for this purpose a preparation of hydrogen peroxide must be used that is perfectly free from acid, — in fact, perhydrol, otherwise there is danger of the teeth breaking off after they have been bleached.

In the treatment of meningococcus carriers, perhydrol is said by H. Bethge to be superior to other disinfectants, because it acts more rapidly. At any rate his investigations have shown that the desired result is obtained most rapidly with perhydrol treatment, preceded by irrigation of the naso-pharynx. The good action of perhydrol is due to its high disinfectant power, and to the mechanical cleansing of the crypts and recesses of the mucous membranes by the oxygen given off on the use of perhydrol. In epidemics Bethge's suggestion may therefore be recommended.

As perhydrol is undoubtedly the most harmless remedy for wounds, it deserves trial in the after treatment of operations on the gums and tonsils. A. Baurowicz does not allow his patients to gargle during the first 4 or 5 days after the operation, lest the wound be lacerated. The mouth and throat are then washed out with perhydrol solution (4:100).

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Bethge, Deutsche medizinische Wochenschrift 1910, No. 2.  
Baurowicz, Monatsschrift für Ohrenheilkunde und Laryngo-Rhinologie 1910, No. 11.

In ophthalmic practice the communications of Sydney Stephenson and B. Sylla are of interest. Stephenson obtained very satisfactory results with a mixture of equal parts of perhydrol and sterile water in blepharitis, suppuration of the lachrymal sac, and septic corneal ulcers. In his experience the remedy gave excellent results in ophthalmia neonatorum, in which it expels the pus from the children's eyes and appears to have a curative action as well. Sylla used perhydrol solution (1 to 3 p.c.  $H_2O_2$ ) in conjunctivitis Meibomiana as a diagnostic, having observed that the swelling passes off and the conjunctiva becomes transparent after the instillation of the solution. Embedded in the tissue are then seen abnormal, punctiform foci and white spots. These disappear as healing advances. The appearances produced by perhydrol may furnish a clue to the existence and cure of diseases of the conjunctiva; hence Sylla's experiments should be continued.

In acute and chronic gonorrhœa Skonlsky has used hydrogen peroxide solutions with excellent results. In acute gonorrhœa he injected a 0.8 p.c. solution 4 times a day, but he did not begin the treatment until the inflammation had passed off, — about the third week of the disease. In chronic gonorrhœa he began by injecting a 1.5 p.c. solution, and increased its strength gradually to 3 p.c. The applications were made twice a day, and the patient was required to retain the injected fluid for about 3 minutes. In balanitis perhydrol acts as a real specific. P. Romeo points out that the germs of the disease are anaërobic, and are therefore killed by the oxygen liberated by the hydrogen peroxide. In slight forms of balanitis the author used a 2 p.c. solution, in severe forms of gangrenous balanitis, a 25 p.c. solution.

S. Flexner suggests the use of perhydrol in poliomyelitis for the reason that the poison of the disease is

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Stephenson, *The Ophthalmoscope* 1910, 1<sup>st</sup> October.

Sylla, *Wochenschrift für Therapie und Hygiene des Auges* 1910, Vol. 13, No. 18, p. 145.

Skonlsky, *Semaine médicale* 1910, No. 30. — *Revue de thérapeutique* 1910, p. 607.

Romeo, *Gazzetta degli ospedali e delle cliniche* 1910, 4<sup>th</sup> October.

Flexner, *Journal of the American Medical Association* 1910, No. 22, p. 1782.



introduced into the organism through the nose, and is therefore best rendered harmless in the nose. For this purpose he found a mixture of 1 part of perhydrol and 30 parts of water suitable for disinfecting the interior of the nose. This treatment is said to have a very favourable effect on the course of the disease.

The value of perhydrol in the treatment of wounds has been further confirmed by the work of Werner and Jaenecke. Jaenecke used it in horses with severe wounds caused by blows of the hoof or pressure of the saddle; his results were entirely satisfactory. Werner extols the cleansing and disinfectant action of the remedy in suppurating wounds and fistulæ, while he draws attention to the good effects of the 1 p. c. solution in corneal injuries and inflammation of the conjunctiva. The 3 p. c. solution (perhydrol 1, water 9) was particularly useful for loosening crusts, while a mixture of equal parts of perhydrol and glycerin proved a valuable remedy for badly granulating wounds. F. Kuntsschik has also obtained remarkable results with perhydrol in fistulæ. He injected a 3 p. c. solution every day. After 10 days the fistula closed and did not reopen subsequently. An equally good result was obtained with perhydrol treatment in a cervical fistula.

The possibility of using perhydrol for practical chemical analysis has been extended by E. Schær's observations. The author's experiments show that a mixture of 1 c. c. of perhydrol with 10 c. c. of strong sulphuric acid may be used with advantage as a test for alkaloids. Perhydrol and sulphuric acid become warm when mixed; the mixture must be allowed to cool before use. The substance to be tested is then added to the reagent in quantities of 5 to 10 milligrammes, preferably in the dry state. Quinine gives a lemon or canary yellow colour, berberine a cherry red colour, hydrastine a chocolate colour, emetine a dark orange and nicotine a blood red colour. The colour is sometimes increased in intensity by the addition of small quantities of platin sol. Further, a mixture of hydrochloric acid and perhydrol may be used, after the addition of a little solution of

Werner, Zeitschrift für Veterinärkunde 1910, No. 7, p. 337.

Jaenecke, Zeitschrift für Veterinärkunde 1910, No. 7.

Kuntsschik, Deutsche tierärztliche Wochenschrift 1910, No. 38.

Schaer, Archiv der Pharmazie 1910, No. 6, p. 458.

chlorine or bromine, for the detection of caffeine and theobromine.

### Periplocin.

This glucoside is obtained from the *Periploca græca*; it was recommended by Lewaschew for heart disease in place of digitalis drugs, but it has found little favour, probably because the subcutaneous injections are painful. For this reason Cholewa has suggested its endonasal use. Analogy with other drugs would have led us to expect that the intravenous application would be painless and more rapid in its action than the subcutaneous or the endonasal exhibition. This assumption has been confirmed in a work by L. A. Silberberg. The author's good results ought to lead to an increased interest in the properties of periplocin.

Silberberg found that the same effects were produced by intravenous injections of periplocin as by other cardiac remedies, i. e., they regulate and accelerate the heart's action. At the same time there is a rise of blood pressure and an increase of diuresis. The increased cardiac activity is particularly obvious in heart disease, while in myocarditis the beats are made regular by it. The constant result of intravenous treatment with periplocin is to increase the heart's activity and to relieve the troublesome subjective symptoms, including attacks of stenocardia, shortness of breath and irregularity of the pulse. The effect follows the injection at once. The special advantages of periplocin over other cardiac remedies, such as digitalis and strophanthin, are stated by Silberberg to be the painless nature of the intravenous injections and the absence of cumulative action. Neither did the author observe any other secondary effects.

The average therapeutic dose is given by Silberberg as 0.001 gramme ( $\frac{1}{64}$  grain). His experimental tests and his clinical observations show that periplocin is better suited for intravenous injection than strophanthin or digalen. The latter certainly increases the cardiac activity, but it has the disadvantage that it requires to be given in very large

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Lewaschew, Merck's Reports 1898, p. 124.

Cholewa, Merck's Reports 1904, p. 151.

Silberberg, Dissertation Odessa 1909.

doses, and this is fraught with difficulties when there are sclerotic changes in the veins.

For intravenous injection the solution suggested by Lewaschew is probably suitable:

Rp. Periplocin	0.01 gramme ( $\frac{1}{6}$ grain)
Sod. chlor.	0.6 gramme (9 grains)
Aq. dest.	10 grammes ( $\frac{1}{3}$ oz)

Sterilise: 1 c. c. to be injected intravenously.

### Peristaltin.

Peristaltin is said by P. Pietsch to be a glucoside from the bark of the cascara sagrada, of the chemical formula  $C_{14}H_{18}O_8$ . It is insoluble in ether, benzol and petrol ether, but is readily soluble in water and alcohol, the resulting solution has an acid reaction. It is not an anthracene derivative; Pietsch describes it as a drug occupying a special place among the purgative remedies; we should not expect it, therefore, *a priori*, to resemble anthracene in its pharmacological action. Thus it is stated that aloin, injected subcutaneously into animals, may give rise to acute or chronic nephritis; peristaltin, however, was found by the author to do no harm to the kidneys of dogs, cats or horses. In rabbits only does a dose of peristaltin sufficient to produce diarrhoea give rise to symptoms of nephritis as well. In a medium sized dog, a dose of 1 gramme, given by mouth, causes a motion; in a horse a dose of 30 grammes is just large enough to act. As a rule peristaltin resembles the members of the anthracene group in that the action does not come on for several hours when the drug is given by mouth. The action is fairly gentle. In the course of the day, two or three fairly thin stools are obtained. Healthy kidneys are not inflamed, except in rabbits. Peristaltin has one feature that places it ahead of the pharmacologically allied substances—it may be given subcutaneously with good results and without injuring the kidneys.

### Physostigmine.

O. Loewi and G. Mansfeld sought to ascertain the mode of action of physostigmine by pharmacological means,

Pietsch, *Therapeutische Monatshefte* 1910, No. 1, p. 35.

Loewi - Mannsfeld, *Archiv für experimentelle Pathologie und Pharmakologie* 1910, Vol. 62, No. 2, p. 180.



and carried out experiments to determine whether the well known action of the remedy was due to stimulation of the peripheral system, or to an increase in the irritability of this system for stimuli (whether nervous or chemical). They came to the following conclusions: Physostigmine increases the sensitiveness for nerve stimuli of the cranial and sacral autonomous innervated organs. This was demonstrated in the case of the striated muscles, the salivary gland, the bladder, and the heart. The authors conclude that the peripheral effects of physostigmine are due to this increased sensitiveness, whereby stimuli that would, normally, produce no effect become effective. Their results show that the use of physostigmine serves to demonstrate that certain organs possess autonomous nerve tone. In this category are the sphincter iridis and the salivary gland. This is apparently absent in the bladder.

G. Winqvist gave physostigmine salicylate in doses of 0.0003 to 0.0006 gramme ( $\frac{1}{200}$ — $\frac{1}{100}$  grain) in neurasthenia. The disease ran a favourable course, and he explains this by assuming that the physostigmine causes powerful contractions in the muscles of the intestines and vessels, aiding the complete assimilation of the food by regulating the bowels and improving the circulation. The remedy also has its effect on the mind, improving the patient's general frame of mind. For this reason he was also successful with physostigmine in certain psychoses.

Investigations on the action of physostigmine when given subcutaneously after laparotomy were carried out by Solowjew; he found that the intestinal peristalsis could be completely restored by injecting fresh solutions. Doses of 0.001 to 0.003 gramme ( $\frac{1}{64}$ — $\frac{1}{20}$  grain) could be given daily without endangering the life or the health of the patient. This result is obtained both in local or progressive peritonitis and in post-operative intestinal paresis. No contra-indication is afforded by the condition of the bowel, or by the nature of the operation performed upon it. In view of the lack of trustworthy remedies for post-operative intestinal

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Winqvist, Finska läkaresällsk. handlingar Vol. 51, senare halffaret, p. 631, Nordisches medizinisches Archiv 1910, II, No. 1, p. 40.

Solowjew, Petersburger medizinische Wochenschrift 1910, No. 32, p. 423.

inertia, the author recommends the further trial of phystigmine injections.

### **Potassii bichromas.**

Potassium bichromate has so far not been extensively used for internal administration, principally because the salt is considered to be very poisonous. Kobert believes even now that the continued internal administration of chromates may cause chronic poisoning. The chromium compounds must possess therapeutic properties, however, for from time to time chromium treatment finds a champion. Last year I reported\*) on the use of chromium sulphate. With regard to the use of potassium bichromate, about 20 years ago J. E. Güntz recommended the so-called chromium water, a solution of potassium bichromate, for the treatment of syphilis. In diphtheria it is also said to be of good service. The remedy came into discredit probably because Güntz recommended it without due criticism, and did not support his assertions by sufficient objective evidence. I do not know whether it has been completely forgotten. Recently H. Kellerhals wrote an account of Güntz's method of treating syphilis with chromium, and Helbig writes on the same subject. Helbig considers that the idea that the chromium salts are dangerous is exploded. Hence it is permissible to try chromium water (potassium bichromate solution) in suitable doses. In his opinion it is not possible to state special indications for its use, any more than in the case of arsenic and iodine. The most suitable cases for treatment with potassium bichromate are patients who have had repeated relapses after the use of mercury, or have been unable to stand mercury treatment because of complications such as tuberculosis, carcinoma, diabetes, etc. Chromium is not superior to iodine or arsenic as regards rapidity of action, hence its effects are not evident until several weeks have passed. Relapses frequently occur, but there is nothing to prevent the repetition of the potassium bichromate treatment,

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Kobert, Intoxikationen 1906, 2. Auflage, II., p. 55.

\*) See Merck's Reports 1909, p. 164.

Güntz, Wiener medizinische Zeitung 1891. — Chromwasser gegen Syphilis, Leipzig 1902, published by E. Haberland.

Kellerhals, Ärztliche Rundschau 1909, p. 617.

Helbig, Ärztliche Rundschau 1910, p. 157.

for chronic poisoning appears never to occur. Helbig gives the following directions for chromium water:

Rp. Pot. bichrom.            0.03 gramme ( $\frac{1}{2}$  grain)  
Sacchar. lact.            0.5     „     ( $7\frac{1}{2}$  grains)  
M. Ft. pulv. Mitte XXX. Sig.: As directed.

These powders keep a long time if suitably stored (especially if protected from moisture). They are taken as follows: A powder is emptied into a bottle of soda water from which a glassful has been previously poured out, and is dissolved by shaking. This solution is taken after breakfast, after lunch and after dinner. It is not absolutely necessary to use aerated water for the solution of the powder; 600 c. c. (20 oz) of ordinary drinking water may be used. The amount of fluid for one dose (0.01 gramme [ $\frac{1}{6}$  grain]) should not be less than 200 c. c. ( $6\frac{2}{3}$  oz). Helbig considers this treatment appropriate in late forms, especially in doubtful or complicated cases.

J. B. Tomblson found the administration of potassium bichromate of use in phthisis. He gave it with some success 2 to 3 times a day in doses of 0.015 gramme ( $\frac{1}{4}$  grain) in a wineglassful of water.

### Potassii permanganas.

In whitlows, cellulitis, abscesses and furuncles, P. Blumm found the following method of treatment of use: The abscess is freely opened and the pus removed. The cavity is then completely filled with crystals of potassium permanganate, and undiluted wood vinegar is poured upon it, when a free evolution of oxygen takes place. The wound is dressed with compresses soaked in a 6 p. c. dilution of wood vinegar. After 24 hours the wound is found to be filled with greasy, crumbly particles which are best removed by washing them out with a stream of water. The wound ought then to be perfectly clean and free from necrotic debris, and it should heal rapidly. J. Fink also used the crystalline salt in various ulcers. He applied it in such a way that the healthy skin was protected as far as possible from contact with it. He achieved this by using a number of strips of strapping

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Tomblson, *Lancet* 1910, No. 4551, p. 1484.

Blumm, *Münchener medizinische Wochenschrift* 1910, No. 6, p. 310.

Fink, *Münchener medizinische Wochenschrift* 1910, No. 4, p. 186.



one over the other. The method is said to be of good service in cancrroids, fungus, granuloma, bedsores, ulcers of the leg, angioma cavernosum, keloid, carbuncles, and in small growths in the face such as nævi, angiomata, lipomata, papillomata, etc. In tuberculous fistulæ of bones and joints the author packed the fistulous passage, including the bone itself, with powdered potassium permanganate. For this purpose he used a tube with a funnel-like expansion. With this treatment severe pain was sometimes produced, and lasted about an hour. After 1 to 2 days the dead tissues were thrown off. The fistula becomes clean, and the discharge diminishes; in many cases the fistula closes and heals. This treatment is contra-indicated in recent fistulæ with copious discharge, and in fistulæ in the immediate vicinity of large vessels and nerves. The author has ascertained that the introduction of 2 grammes (30 grains) of potassium permanganate into the deep parts does not cause the least injury. In about 10 p.c. of the cases he found that tuberculous bone disease was cured as a direct result of his treatment. In his experience the introduction of potassium permanganate in substance is better tolerated than the injection of a 5 p.c. solution, which is far more painful, and requires to be repeated every day. L. Neumayer tried Fink's method in 2 cases. In one case the results were very satisfactory, in the other, a deep suppuration of the palm of the hand, there was arterial secondary hæmorrhage. Hence he thinks the application should be avoided in the vicinity of arteries, at any rate in out-patient practice.

F. Becker used powdered potassium permanganate in lupus years ago, and obtained very satisfactory results in severe cases, the cosmetic effects being particularly good. The results, however, were not permanent. The great disadvantage of the application of potassium permanganate powder is the great pain it causes, and in the author's opinion this occurs not only in lupus, but in other skin diseases as well. Becker believes therefore that the potassium permanganate method will not find much favour.

A new method for treating variola is described by W.

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Neumayer, Münchener medizinische Wochenschrift 1910, No. 33, p. 1746.

Becker, Münchener medizinische Wochenschrift 1910, No. 8, p. 412.

Dreyer. It consists in painting the whole body, or at any rate the parts of the body that are covered with pustules, with a saturated aqueous solution of potassium permanganate. This may be repeated several times a day, the object being to disinfect the skin and the suppurating ulcers, and at the same time abolish the unpleasant smell which annoys both the patients and the attendants. This treatment has no effect on the course of the infection, the object being merely to deal with the suppuration and its consequences. Care is needed in case of great cardiac weakness in which the patient's condition might possibly be rendered worse from the absorption of potassium. In such cases sodium permanganate might presumably be suitable.

For the analysis of urine a new reaction, discovered by M. Weiss, is of interest, viz., the permanganate or urochromogen test which requires a 0.1 p.c. aqueous solution of potassium permanganate. The urine to be tested is filtered if necessary, and diluted with double the quantity of water. Two test tubes are half filled with this dilution, and 3 drops of potassium permanganate solution are added to one test tube. If the urine contains urochromogen the yellow colour deepens, and this is easily recognised by comparing it with the other test tube. The intensity of the colour is proportional to the intensity of Ehrlich's diazo-reaction\*). If the result of the reaction is doubtful the test is repeated with a mixture of equal parts of urine and water. By means of this reaction the amount of urochromogen may be estimated, and the author gives directions for this purpose.

#### Potassii tartras acidus.

The treatment of cirrhosis of the liver by acid potassium tartrate was suggested by Eichhorst:

Rp. Decoct. Althææ rad.	10:180 ( $\frac{1}{3}$ :6 oz)
Pot. tart. acid.	15.0 ( $\frac{1}{2}$ oz)
Syrup.	20.0 ( $\frac{2}{3}$ oz)

Sig.: One tablespoonful every two hours.

Dreyer, Münchener medizinische Wochenschrift 1910, No. 31, p. 1642.

Weiß, Medizinische Klinik 1910, No. 42, p. 1661.

\*) See Merck's Reagenzien-Verzeichnis 1908, p. 68.

Eichhorst, Merck's Reports 1909, p. 350.

This treatment was tested by J ü s g e n in a number of cases. He found that slight cases of cirrhosis of the liver, with no cardiac or renal complications, were quickly relieved by taking acid potassium tartrate, and the good result was not diminished by the presence of moderate disease of the kidneys. Equally good results were obtained in severe cirrhosis with ascites and oedema, provided there was no disease of the heart and kidneys. The threatening symptoms disappeared in a very short time, without puncture. If the heart is acting well, a successful result is obtained in severe cirrhosis even complicated by moderate disease of the kidneys. The improvement is not purely symptomatic, it is causal, and in proof of this the author mentions the fact that the bile pigments and the urobilin disappeared from the urine after the commencement of the treatment. The diuretic action continues for some time after the administration of the tartrate has been left off. When there is disease of the cardiac muscle and severe inflammation of the kidneys the tartrate may fail to act.

Its antiseptic and absorbent properties make acid potassium tartrate useful as an external remedy for anthrax. Lupo and Miranda made a cross-wise incision in the anthrax pustule, separated the edges and filled the cavity with sterile gauze impregnated with acid potassium tartrate. With this treatment the fever subsided quickly, and the general condition improved. Every four days the wound was washed out with sterile water, and the gauze dressing was renewed. This was followed by alternate washing with water and 0.1 p.c. corrosive sublimate solution. This treatment has the advantage over cauterization of being less painful, and giving better cosmetic results. The authors point out particularly that acid potassium tartrate in the form of a powder is far more efficacious than the same salt in aqueous solution.

### **Protargol.**

In using protargol for the prophylactic treatment of gonorrhœa, Heilig frequently observed irritant symptoms,

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Jüsgen, *Klinisch-therapeutische Wochenschrift* 1910, No. 35, p. 837.  
Lupo-Miranda, *Klinisch-therapeutische Wochenschrift* 1910, No. 24, p. 587.

Heilig, *Medizinische Klinik* 1910, No. 25.



such as burning pain on micturition: he was also doubtful as to the value of the prophylactic instillation of solutions of protargol in glycerin (1 and 4), for in the cases treated prophylactically with success it could not be proved absolutely that gonorrhœa would have broken out but for the protargol treatment. E. Bäumer is convinced, however, of the value of prophylactic treatment when gonorrhœa threatens. He attributes the ill effects described by Heilig to the use of glycerin that is free from water. If water is used, or a mixture of glycerin and water, for dissolving the protargol, the irritant effects are greatly reduced. They could be prevented by the addition of alypin to the injection fluid. This improved prophylactic agent is composed by Bäumer thus:

Rp. Protargol	1.0 gramme (15 grains)
Solve in aqua destill. frigida	6.0 grammes (100 min.)
Adde alypin nitr.	0.25 gramme (4 grains)
Solut. in aq. dest.	4.0 grammes (70 min.)

The alypin solution must be added to the finished protargol solution. In this new form it is said that the prophylactic treatment of gonorrhœa with protargol may be used continually even in the most sensitive patient. Delbet prescribes a dilute solution of protargol which is said to cause no trouble. The bladder and urethra are first washed out with a 0.025 to 0.05 p. c. aqueous solution of oxycyanide of mercury, whereupon an injection is given at once consisting of 5 c. c. of a mixture of equal parts of glycerin and of a 5 to 10 p. c. protargol solution. This treatment is repeated every day or two. Chrzelitzer attributes the inflammation occasionally seen after the use of protargol solution to the fact that it has been prepared with the aid of heat, or else that it has been kept too long, and is partially decomposed. For this reason he prescribes not more than 100 c. c. of a 0.5 to 1.5 p. c. solution, enough for a few days, and by this means the patient continues to receive fresh solutions. There are advantages in using warm solutions; the author accordingly recommends the following way of preparing the injections or lotions: The protargol is spread upon cold water and left

Bäumer, *Medizinische Klinik* 1910, No. 29.

Delbet, *Münchener medizinische Wochenschrift* 1910, p. 51.

Chrzelitzer, *Berliner klinische Wochenschrift* 1910, No. 37.

for 1 to 1 $\frac{1}{2}$  hours, when solution will take place of its own accord. This solution is made of the required strength; it is mixed, in an irrigator, with water warmed to 45° C., and used at once. It must not be warmed repeatedly by placing it in water. The proper concentration for the protargol solution is 1 to 3 p. c. Hot protargol solution was also used by Chrzelitzer with satisfactory results in soft sores. The ulcer was washed under high pressure with a 2 p. c. solution (using 2 litres once a day); 10 p. c. protargol-vaseline was then inserted. With this treatment the ulcers soon became clean, and they healed in the shortest possible time. In gonorrhœal cystitis protargol is also said to give good results.

A. Ramacci has followed Hesky in using protargol with excellent results in children suffering from acute gastro-enteritis, catarrh of the large intestine, and acute and chronic catarrh of the small intestine. By avoiding the use of albuminous food and giving 0.6 to 1 gramme (9—15 grains) of protargol in aqueous solution daily, he soon obtained successful results, even in cases which had failed to yield to the usual lines of treatment. The results of A. Cantani agree with this; in various gastric affections usually treated by silver nitrate he obtained very satisfactory results by washing out the stomach with a 0.2 p. c. solution of protargol.

### **Pyocyanase.**

J. Hofbauer is known to have made a previous attempt to treat gonorrhœa by the local application of pyocyanase. His results were negative, however, for the action did not extend deeply enough. Recently A. Spatz has tested the action of the remedy, with equally unsatisfactory results. The number of gonococci was not affected by the instillation of pyocyanase, neither were the symptoms or inflammation relieved. On the contrary the preparation appears apt to cause toxic symptoms; at any rate the author noted in two cases of acute gonorrhœa a rise of tempera-

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Ramacci, *La Pediatria* 1909, No. 8.

Hesky, *Wiener medizinische Zeitung* 1908, No. 7. — Merck's Reports 1908, p. 306.

Cantani, *Gazzetta degli ospedali e delle cliniche* 1910, No. 138.

Hofbauer, *Merck's Reports* 1908, p. 282.

Spatz, *Wiener medizinische Wochenschrift* 1910, No. 40.

ture and a feeling of weakness after the use of the remedy. Pyocyanase seems to give better results in soft sores. A. Hatzfeld cleansed the sores and then treated them with pyocyanase sprays and sterile gauze. Buboës were incised, and plugged with strips of gauze soaked in pyocyanase; they were then sprayed till they healed. The ulcers became clean in a few days and then cicatrised rapidly. In case the sprays cause burning and severe pain, the previous application of 3 p. c. cocaine solution is advisable. No other secondary effects were ever observed by the author. As compared with the use of caustics and powders, the application of pyocyanase has the advantage, in Hatzfeld's opinion, of sparing the healthy tissues from attack. Pyocyanase does not cause mucus and discharge to coagulate; its effect is rather to dissolve them and to accelerate the cure by exciting cell production. As soon as the treatment is commenced the stage of destruction is checked, and improvement continues from day to day. Further, the appearance of buboës was always prevented by pyocyanase, provided the inguinal glands were not already swollen and painful.

V. Guttman reports good results with pyocyanase in tonsillitis lacunaris. A pyocyanase spray was applied once a day only, with the result that the discharge disappeared from the throat on the following day in the great majority of cases. The other subjective and objective troubles were also quickly relieved.

### Pyramidon.

The value of pyramidon in typhoid fever was extolled some time ago by Valentini. This has been confirmed in a paper by L. Jacob, who describes the results obtained with the drug in Moritz's Clinic in Strassburg. Jacob prescribed a mixture of the following composition:

Rp. Pyramidon	2.0 grammes (30 grains)
Syrup.	20.0 „ ( $\frac{2}{3}$ oz)
Aq. dest. ad	200.0 „ ( $6\frac{2}{3}$ oz)

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Hatzfeld, *Therapeutische Monatshefte* 1910, No. 11.

Guttman, *Fortschritte der Medizin* 1910, No. 46. Casopis  
lekaru Ceskych 1910, No. 4.

Valentini, *Merck's Reports* 1903, p. 153.

Jacob, *Münchener medizinische Wochenschrift* 1910, No. 33.



Of this, 10 grammes ( $1\frac{1}{3}$  oz) were given every 2 hours from 6 a. m. to midnight, so that 1 gramme (15 grains) of pyramidon was given within 24 hours. With this treatment the fever usually came down a degree or more, and assumed a milder course or subsided altogether if the treatment were continued long enough. Still more striking was the action of pyramidon on the general condition, for the drowsiness, headache, restlessness and the heavy typhoid state ceased, the sensorium cleared and feeding became considerably easier. A point worthy of special mention is Jacob's observation that patients under treatment with pyramidon never soiled their clothes with urine or fæces; thus the attendants incur far less danger of infection. The treatment was usually continued for 10 to 20 days; occasionally as long as 35 days, and once as long as 41 days, without setting up unpleasant secondary symptoms in a single case. A few patients sweated profusely during the first days, but this did not necessitate an interruption of the treatment. It was continued, even on the occurrence of hæmorrhage, or when other drugs had to be used, such as digitalis, caffeine or camphor. If a hæmorrhage caused a great fall of temperature and accelerated pulse, then alone was the pyramidon discontinued. To tend the skin, and to prevent pulmonary complications, cool sponging and Priessnitz' compresses were applied, though no baths were given. As compared with other methods of treatment, Jacob's method is shown, by the results he has collected during several years, to have led to a marked fall in the death-rate; it therefore deserves the attention of medical men.

Pyramidon is also found of use in dysphagia due to laryngeal tuberculosis. The following solution is used\*):

Rp. Pyramidon	2.0 grammes (30 grains)
Cocain. hydrochlor.	0.2—0.5 gramme ( $3-7\frac{1}{2}$ grains)
Morph. hydrochlor.	0.1—0.2 gramme ( $1\frac{1}{2}-3$ grains)
Aq. laurocer.	60.0 grammes (2 oz)

A teaspoonful of this in a glass of water three-quarters full is used as a spray for inhalation.

Pouchet found pyramidon an excellent remedy for toxic neuritis, headache in anæmic subjects, and the pains

\*) Le Larynx, l'Oreille et le Nez 1910, No. 2. — Presse médicale 1910, p. 440.

Pouchet, Revue internationale de médecine 1910, 324.

of tabs. It is also of good service in migraine and hyperthermia. The author recommends the following prescription:

Rp. Pyramidon 1.0 gramme (15 grains)

Syrup. aurant. cort. 25.0 grammes ( $\frac{5}{6}$  oz)

Aq. dest. 75.0 grammes ( $2\frac{1}{2}$  oz)

Sig.: To be taken within 24 hours, a tablespoonful at a time.

Better results are said to be obtained by a combination of pyramidon with quinine hydrobromide. The author recommends the administration of a powder, 5 to 10 times a day, composed of 0.05 gramme ( $\frac{3}{4}$  grain) of pyramidon, and 0.1 gramme ( $1\frac{1}{2}$  grains) of quinine hydrobromide.

### Pyrogallol Dimethyl Ether.

Pyrogallol dimethyl ether,  $\text{OH} \cdot \text{C}_6\text{H}_3 \cdot (\text{OCH}_3)_2$ , forms colourless crystals, melting at 51 to 52° C.; they are soluble in 50 parts of water. On oxidation it is converted into cœrulignone though with some oxidising agents there appears to be an intermediate product of an intense colour. This is obtained, as J. Meyerfeld has shown, with chromic acid, ferric salts and nitrous acid, but not with hydrogen peroxide and nitric acid, provided very dilute solutions are used. Hence an aqueous, freshly prepared 2 p.c. solution of pyrogallol dimethyl ether may be used as a test for chromic acid, salts of oxide of iron, nitrous acid and nitrites. If we take a colourless fluid containing traces of these compounds, acidify it with sulphuric acid and add the reagent, a yellow, or reddish colour appears; this may be rendered still clearer by shaking with a little chloroform, for the colouring matter passes into it. Ether cannot be used for the purpose.

In the case of chromic acid the yellow colour is obtained with only 0.00005 p.c. and with the aid of chloroform,  $\frac{1}{1000}$  to  $\frac{2}{1000}$  milligramme may be detected. Hence this reaction is far more sensitive than the well known blue reaction with hydrogen peroxide and ether. In the case of iron oxide salts, the author found the reaction just about as sensitive as the thiocyanate reaction. The reaction for nitrous acid is about equal in sensitiveness to the potassium iodide and starch reaction. With it  $\frac{8}{1000}$  milligramme may be detected in 5 c. c. of water. If the author's statement is correct that

Meyerfeld, Chemiker-Zeitung 1910, No. 107, p. 948.

very dilute nitric acid does not give the reaction, the pyrogallol dimethyl ether solution will be highly suitable for distinguishing between nitric and nitrous acids.

### Quinine.

Good prospects of treating pemphigus are held out in the communications of R. Bergrath and Leibkind. The authors gave 0.5 gramme ( $7\frac{1}{2}$  grains) of quinine hydrochloride 3 to 4 times a day in this disease with better results than they had obtained by any other medicinal treatment. A few days after the commencement of quinine treatment the improvement begins in the vesicles, and their number diminishes. In the first days of treatment the temperature rises to  $38.5^{\circ}\text{C}$ . and this may be due to a reaction of the organism to the poison of the disease. On further treatment with quinine the vesicles disappear entirely, and there is a decided improvement in the general condition, with a gain in weight. By long-continued intermittent quinine treatment Bergrath believes it will be finally possible to extinguish the pathological process giving rise to pemphigus. The internal treatment by quinine must be accompanied by the application of external remedies such as ichthyol, xeroform, zinc oxide, etc.

Quinine is of use in other skin affections. Thus G. T. Jackson reports that doses of 0.5 to 0.6 gramme ( $7\frac{1}{2}$  to 9 grains) of quinine every 4 hours gave excellent results in exfoliative dermatitis, and produced no harmful secondary effects. With due regard for individual susceptibility quinine should also be of good service in pityriasis rubra, to judge by the cases communicated by G. Pernet.

With regard to the use of quinine as a local anæsthetic we have the papers of L. J. Hirschman, W. O. Green, MacCampbell, Hertzler, Brewster and Rogers.

Bergrath, *Münchener medizinische Wochenschrift* 1910, p. 18.

Leibkind, *Münchener medizinische Wochenschrift* 1910, p. 19.

Jackson, *Journal of cutaneous diseases* 1910, January. — *Monatshefte für praktische Dermatologie* 1910, Vol. 50, p. 256.

Pernet, *ibid*.

Hirschmann, *Lancet-Clinic* 1910, 9<sup>th</sup> July.

Green, *Journal of the American Medical Association* 1910, 11<sup>th</sup> June.

Campbell, *Journal of the American Medical Association* 1910, 14<sup>th</sup> May.

Hertzler, Brewster, Rogers, *The Prescriber* 1910, p. 19. — *Klinisch-therapeutische Wochenschrift* 1910, p. 96.



These show that subcutaneous injections of a 1 to 2 p.c. solution of quinine hydrochloro-carbamide and the local application of a 10 to 20 p.c. solution occasionally have a better anæsthetic action than cocaine. Quinine is said to be specially useful in operations at the anus where its analgesic action extends to 7 to 10 days with the agreeable result that the pain usually following such operations remains absent. A better solution than the urea quinine solution is given by F. Chavanne:

Rp. Acid. carbol.	2.0 grammes (30 grains)
Menthol	2.0 „ (30 grains)
Quinin. hydrochl.	1.5 „ (24 grains)
Adrenalin	0.005 gramme ( $\frac{1}{12}$ grain)

If a few drops of this are placed on a tampon of wool and the mucous membrane of the throat is swabbed with it, it becomes white, shrinks and becomes insensitive. Immediately after this manipulation it is said that deep cauterization may be carried out without pain. Chavanne states that the solution has no caustic action.

Petty also speaks well of the external use of quinine, especially if there is any difficulty in administering it internally, or if its bitter taste leads to a refusal to take it (as in children). In malaria the author applied a solution of 1 part of quinine bisulphate in 4 parts of glycerin locally and says that he obtained the same results as by the internal administration of quinine. He directs that the selected part of the skin be first cleaned with water to facilitate absorption, 4 to 8 grammes (70—135 min.) of the solution being then applied. This may be repeated every 3 to 4 hours.

In hæmoptysis in tuberculous subjects Justmann recommends tannate of quinine in doses of 0.5 gramme ( $7\frac{1}{2}$  grains) together with 0.01 to 0.015 gramme ( $\frac{1}{6}$ — $\frac{1}{4}$  grain) of dionin, and in whooping-cough L. Berliner recommends a quinine ointment for endonasal treatment. For this purpose an ointment is used, varying with the age of the child, and consisting of 1 to 2.5 grammes (15—40 grains) of quinine and 10 to 15 grammes ( $\frac{1}{3}$ — $\frac{1}{2}$  oz) of lard. Of this

Chavanne, *Klinisch-therapeutische Wochenschrift* 1910, No. 50, p. 1253.

Petty, *Practical Medicine* 1910, No. 10, p. 194.

Justmann, *Przegląd lekarski* 1910, No. 6.

Berliner, *Münchener medizinische Wochenschrift* 1910, p. 360.

a quantity the size of a pea is introduced 3 to 4 times in each cavity of the nose by means of a glass rod. The child is then placed on its back to enable the ointment to flow back. This method is said to act better the younger the child.

In the treatment of trypanosomiasis quinine has as yet found no extensive use, for since the experiments of Mesnil and Brimont it has been thought to have no action on the trypanosomes. More recent experiments on mice have been performed by Morgenroth and Halberstädter. These show that the alkaloid does exert some action on these parasites, at any rate it has a prophylactic effect. The action is evident if subcutaneous injections are given at the same time as the animal is infected. A single injection, however, has no appreciable prophylactic action, even though the dose of quinine is large enough to endanger life. It is necessary to repeat the injections for several days. The authors were led to surmise that a single injection interfered with the multiplication of the trypanosomes, but this soon left off unless more quinine were injected. Although smaller doses appear sufficient to continue the interference, still the doses of quinine for the first effect are very large and approach the lethal dose. This fact, added to the inconstancy of the results observed by the above named authors, leaves little prospect of the successful use of quinine in trypanosomiasis, although a prophylactic action has been proved to exist.

Finally, attention must be drawn to the recommendation by Lemansky of quinine for the treatment of hyperthermia in children; he prescribed suppositories consisting of 0.3 gramme (5 grains) of quinine hydrobromide, 0.05 gramme ( $\frac{3}{4}$  grain) of antipyrine, 0.05 gramme ( $\frac{3}{4}$  grain) of phenacetin and 2 grammes (30 grains) of oil of theobroma.

### Ragit.

Under the protected name of "Ragit" I issue several preparations made at the suggestion of E. Marx. They are intended to simplify the preparation of nutrient media

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Morgenroth-Halberstädter, Berliner klinische Wochenschrift 1910, p. 646.

Lemansky, Riforma medica 1910, No. 28.

Marx, Münchener medizinische Wochenschrift 1910, No. 7, p. 361.

such as are used in bacteriological laboratories, and by bacteriologists when travelling.

Ragit agar consists of powdered agar-agar, peptone and Maggi's granulated meat broth, so proportioned that 42 grammes of the preparation with a litre of water form a nutrient agar which is easily filtered, while all bacteria grow upon it just as well as upon nutrient media prepared from fresh meat. To prepare a litre of nutrient agar, it is merely necessary in future to boil 42 grammes of ragit agar with a litre of water for an hour in a steamer, to filter as hot as possible and to store it suitably. If degrees of alkalinity be desired differing from the usual, they may be obtained by the addition of normal caustic soda solution as required.

Ragit broth consists of peptone and Maggi's granulated meat broth so proportioned that 20 grammes, boiled with a litre of water, form a nutrient broth upon which most bacteria grow as readily as upon broth prepared from fresh meat.

To simplify the preparation of Endo's nutrient media (for typhoid examinations, etc.), the so-called Endo tablets are useful. Each tablet contains the amount of sugar of milk, sodium sulphite, sodium carbonate and fuchsine required by Endo's formula for the preparation of 100 c. c. of neutral agar. A tablet dissolved in 100 grammes of ragit nutrient agar gives us "Endo-agar" as used for typhoid examinations. If it is desired to use a nutrient agar prepared from ordinary meat broth, this must be accurately neutralised before adding the tablet.

The great simplification and saving of time resulting from the use of these preparations in the making of nutrient media should speedily lead to their introduction in all bacteriological institutes. They have been specially tested by F. Sparmberg and Tamie Amako, who have fully confirmed their utility.

### **Resorcin.**

In treating inflamed regions with alcohol dressings, J. Schäffer seeks to enhance the good effects of alcohol

Sparmberg-Amako, Zentralblatt für Bakteriologie 1910, Vol. 56, No. 1.

Schäffer, Berliner klinische Wochenschrift 1910, No. 19, p. 890.  
(See the article "Alcohol" p. 84.)



by the addition of resorcin. Strikingly good results are obtained with relatively dilute spirit in preventing, and dissipating suppuration. Thus he found an addition of 2 to 3 p. c. of resorcin to 50 p. c. alcohol very useful, without inflaming the skin. In furuncles, inflamed infiltrations of the skin, inflamed inguinal glands, para-urethral infiltration, epididymitis, gonorrhœal arthritis, para-urethral abscesses, in fact in all kinds of acute suppuration treated by the author, the following combined method of treatment by alcohol and warmth gave very good results. Twice a day, for 1 to 2 hours, he prescribes hot compresses and seeks to keep up the resulting hyperæmia and lymphatic flow at its maximum in the intervals by applying a dressing of resorcin-spirit of the following composition:

Rp. Resorcin 4.0 grammes (60 grains)  
Alcohol (40 p. c.) ad 200.0 „ (6 $\frac{2}{3}$  oz)

This relatively weak alcohol suffices because we have merely to keep up the flow of blood and lymph, and not to effect it. If the skin can bear it, the concentration of the alcohol may be gradually increased to 50 p. c. The applications are made as for moist dressings, i. e., with an impervious covering, the dressing being changed twice a day. With this treatment Schäffer frequently saw commencing intense inflammation subside, infiltrated furuncles getting well more quickly than usual, and even when a small incision had to be made a rapid cure resulted. The method may be modified to suit the case. Thus in very obstinate chronic inflammation the concentration of the alcohol may be increased, while in regions where the skin is very sensitive, as in gonorrhœal epididymitis, it may be diminished. The treatment is contra-indicated in cases with high fever due to rapid absorption of septic products.

### Sabromin.

Sabromin\*) has been found by Froehlich to give very good results in epilepsy. The dosage must be ascertained by trial in each case, for the quantity required to check the attacks, or to reduce their frequency, may vary from case to case, as with all bromine preparations. As

\*) See Merck's Reports 1908 and 1909.

Froehlich, *Thérapie der Gegenwart* 1910, No. 2.

a rule the author found doses of 3 to 4 grammes (45—60 grains) sufficient. V. Fragola used the preparation in epilepsy with satisfactory results. In his experience its action is not only prompt but continues for a considerable time, even in old cases. J. Bittner, on the other hand, obtained no definite results in his trials with sabromin in epilepsy in Jaksch's Clinic in Prague. His best results were obtained in neurasthenic conditions. In K. Mitterer's opinion the remedy is of use, not only in epilepsy, but in all cases of increased nerve tension, particularly in restlessness and sleeplessness, and when the nervous system is excited and overwrought. As a rule he gave it between 6 and 7 p. m., and the effect became apparent about 3 hours later. His doses amounted to 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains), and he never gave more than 2 grammes (30 grains) for a single dose. Like others before him, Mitterer draws special attention to the fact that sabromin is well borne. Schott also tried the preparation in epilepsy. In respect to its power of mitigating the attacks, he found it inferior to an equal amount of potassium bromide. Some patients, however, found it beneficial because it agreed with them better than potassium bromide. Schott had no doubt as to the good effect of sabromin in aiding the disappearance of a bromide acne.

The treatment of chorea with sabromin is described by D. J. Macht and Maetzke. They report a case each in which a good result was obtained by the long-continued administration of 3 sabromin tablets daily in one case, and 6 daily in the other. It should be remarked that Maetzke attributes the good effect in great part to the calcium contained in the preparation.

### Safranin.

During an investigation with the so-called sensibilisators, Hasselbalch observed that the well known colour safranin

Fragola, *Il Manicomio* Vol. 20, No. 3, p. 283. — *Clinica Castellana* 1910, No. 3, p. 173.

Bittner, *Prager medizinische Wochenschrift* 1910, No. 21.

Mitterer, *Klinisch-therapeutische Wochenschrift* 1910, No. 44.

Schott, *Deutsche Medizinal-Zeitung* 1910, No. 49.

Macht, *Deutsche medizinische Wochenschrift* 1910, No. 49.

Maetzke, *Deutsche medizinische Wochenschrift* 1910, No. 30.

Hasselbalch-Lindhard, *Biochemische Zeitschrift* 1910, Vol. 27, p. 273.

was decolorised in an alkaline solution on boiling with glucose. This fact has been long known; and has been used in tests for glucose in urine by Crismer, Christopher-Crofton and Kellas-Wethered. It led the author, together with J. Lindhard, to work out a method for the quantitative estimation of glucose. The method is said to have several advantages over the usual methods of estimating glucose. 1. The albumen need not be first precipitated. 2. The self-reduction of the urine, even when not decolorised, is considerably less than is the case in any other known method of estimating sugar in urine; this is due, in part, to the fact that the uric acid and the creatinin do not reduce the alkaline safranin solution. The self-reduction, in the case of the safranin method, is a quarter as much as that in Bang's titration method with urine that has not been decolorised. The method of carrying out the determination of glucose by Hasselbalch and Lindhard is as follows:

By means of a pipette or a burette equal parts of an aqueous solution of safranin 1:10,000 and a solution of potassium hydroxide 1:100 are placed in a narrow test tube. To this mixture the sugar solution to be tested is added drop by drop, and the mixture is heated for 3 minutes on a boiling water bath. If the mixture changes from red to yellow, the whole of the safranin has been reduced by the sugar; from the amount of safranin and urine used the amount of sugar in the latter can then be calculated. For each c. c. of the safranin solution (1:10,000), we have to reckon 0.25 milligramme of glucose. For more details of the method the original description should be consulted. The authors state that their method gives the same values as those obtained by the older methods. There is so little self-reduction, however, that the amount of glucose may be estimated with considerable accuracy by a single determination. The safranin solution must be adjusted to a known solution of glucose; it keeps in the dark without the addition of caustic potash. In practice the new method may lead to a difficulty in that we often require, for purposes of control, a sugar solution of known strength, and this always

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Crismer, Christopher-Crofton, Kellas-Wethered, see Merck's Reagenzien-Verzeichnis 1908.

Bang, Biochemische Zeitschrift Vol. 2, p. 271 and Vol. 11, p. 538.



has to be determined in another way to begin with, for it keeps very badly.

### Sajodin.

A. Weiss reports a case in which great pain was occasioned by a twist and burn of a finger joint. He had used other drugs in vain; the pain extended to the entire arm, and the finger swelled up more and more, and became bluish red and sensitive. A Röntgen ray examination showed periostitis and caries of the bone; the author tried the administration of sajodin before resorting to operation. With this treatment the finger became thinner, and in the course of 16 days the pain and inflammation disappeared. This result is attributed by Weiss to the sajodin.

O. Kohlbach used sajodin in fatty heart, bronchial asthma and arterio-sclerosis, alternately with potassium iodide, and obtained very satisfactory results. In syphilis, too, the remedy was of good service. In syphilis his experience has been so favourable that he now always gives sajodin and potassium iodide alternately, for he is convinced that the sajodin makes the potassium iodide agree better\*).

### Salol.

Salol is regarded by A. Denarié to be a very suitable remedy for causing gastric ulcers to cicatrise. He advises, however, that it be not given immediately after blood has been vomited; a preliminary course of treatment should be given. As soon as vomiting has ceased an enema is given, consisting of half a litre of normal saline solution, which the patient has to retain. Every hour he prescribes alternately an ice-cold ergotin mixture with ether and an ice-cold solution of perchloride of iron. On the second day of treatment frozen milk is given, a teaspoonful at a time, and on the fourth day, in the morning, 0.5 gramme ( $7\frac{1}{2}$  grains) of salol in a cup of milk, after which the patient lies on his back for half an hour. This treatment is continued for 30 days. From the 7<sup>th</sup> day of treatment the patient may, as a rule, be given yolk of egg, from the 10<sup>th</sup> day

Weiss, Pester medizinisch-chirurgische Presse 1910, No. 12.

Kohlbach, Wiener medizinische Zeitung 1910, No. 7.

\*) See Merck's Reports 1906—1909.

Denarié, Semaine médicale 1910, No. 47, p. 560.

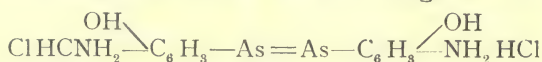
gruel and soup, but meat and bread may not be taken till the end of a month. The salol treatment requires to be continued for months, with suitable intervals, and appropriate diet, until a definite cure has resulted.

A new method of applying salol to the treatment of wounds, a method equally applicable to other antiseptics, is described by Bourlier. His method is to drop upon the wound the most concentrated solution obtainable of salol in chloroform (equal volumes). After the solvent has evaporated, the salol remains as a fine powder, and in this form is said to be particularly effective as an antiseptic. The author proves this by showing that laminaria rods, dipped in this solution, are found to be sterile after 4 days. For this reason he prefers salol-chloroform to iodoform-ether, especially as the former is odourless.

### Salvarsan. (Dioxidiamido-arsenobenzol di-hydrochloride.)

The literature on this new remedy dominates the medical journals of the latter half of the year 1910 in a way that makes it impossible to give anything like a full account here. The remedy has aroused as much attention, in medical and lay circles, as did tuberculin in its time. I must therefore deal, as briefly as possible, with the theoretical and practical views of the Ehrlich-Hata preparation, to give the practitioner the most essential points regarding the use of the preparation, without exceeding the limits permissible in my Reports.

Dioxidiamido-arsenobenzol hydrochloride is a yellow powder, readily decomposed, containing about 34 p. c. of arsenium; it dissolves in water without difficulty to a solution with an acid reaction. It has the following chemical formula:



Therapeutically its chief use is in the treatment of syphilis. An imposing number of workers has taken up the determination of its therapeutic value. We are able to conclude that the preparation will quickly assume a leading place in our list of remedies, even though it has not fulfilled the extravagant hopes voiced upon its introduction. So much may

already be said of it without exaggeration, that it will be of great value if properly used. Its use is limited to subcutaneous, intramuscular or intravenous injection, and owing to its acid reaction it cannot be used in this way without special preparation. So far 3 different ways of applying it have been suggested for the purpose: a neutralised aqueous solution, an alkaline aqueous solution, or an emulsion or suspension in liquid paraffin.

Originally Ehrlich used methyl alcohol in the preparation of the solution; he gave the following directions for preparing the fluid for injection: 0.4 to 0.5 gramme of dioxidiamido-arsenobenzol is stirred up with 0.5 to 1 c. c. of methyl alcohol, dissolved in water, mixed with about 5 to 8 c. c. of  $\frac{1}{10}$  normal caustic soda until neutralised, and made up to 25 to 30 c. c. with water. Fearing the toxic effects of methyl alcohol (See these Reports for 1909, page 100), other methods of preparing the solution were introduced. Thus Citron and Mulzer suggested ethyl alcohol in place of methyl alcohol. They place the required quantity of "606" in a sterile Record Syringe of 15 c. c. capacity, closed at the cannula with a cone, and moisten the preparation with a few drops of alcohol. Hot distilled water is now added up to the mark 5, the piston is inserted into the syringe, the ring is adjusted, and the syringe is well shaken. A clear golden-yellow fluid results. The piston is taken out again and 40 drops of a 10 p. c. suspension of calcium carbonate in normal saline solution are added with constant shaking. A thick, creamy emulsion is obtained, which is injected into the glutei. The object of adding calcium carbonate is to neutralise the solution and to precipitate the free base (the dioxidiamido-arsenobenzol).

Alt has given the following directions for the preparation and injection of the Ehrlich-Hata remedy: In a low measuring cylinder, holding about 50 c. c., a single dose is placed with about 10 c. c. of sterile water. Sterile normal caustic soda is then added\*) until all but a very small amount

\*) The quantity of caustic soda must be determined by the quantity of salvarsan to be used. To prepare the neutral fluid for injection the official directions for use state that every 0.1 gramme of salvarsan requires 0.09 gramme of 15 p. c. caustic soda (about 1 to 2 drops). The preparation is uniformly rubbed up with it, and 5 to 10 c. c. of sterile water



of the substance has dissolved. Water is added to make up 20 c. c., an anæsthetic having been previously added if required. Syringefuls containing 10 c. c. are injected deeply into the right and left gluteal muscles, the piston being advanced slowly.

A less painful injection than this alkaline fluid is said to be the neutral mixture recommended by Michaelis and Wechselmann. It is prepared as follows: A single dose is dissolved in 16 c. c. of very hot sterile water in a measuring cylinder of 50 c. c. capacity. To dissolve it 3 to 5 c. c. of normal caustic soda are added; it is then well stirred and 3 drops of a 0.5 p. c. alcoholic solution of phenolphthalein are added, and enough normal acetic acid to discharge the red colour of the mixture. A fine, yellow suspension of the preparation is obtained by this means. A drop of caustic soda is added, so that the mixture assumes a reddish colour, and the suspension is injected into both glutei.

Jessner gives the following directions: The requisite amount of salvarsan is rubbed to a fine powder in a small, sterile mortar; four times the quantity of a sterile saturated solution (about 8 p. c.) of sodium bicarbonate is poured over it. The mixture effervesces and carbonic acid is liberated, further careful rubbing converts it into an extremely fine emulsion which is neutral, or very faintly alkaline. Sterile normal saline solution is then added to five times the amount of the remedy, making a 10 p. c. emulsion, ready for use. Before drawing it into the syringe the mixture is rubbed up once more. The pain produced by injecting this emulsion is said to be very slight.

Which of these prescriptions to use in preparing the injections must be settled by the individual worker, or by the condition of the patient. In my opinion the best prospects are afforded by the suspension of the "606" in oils, because this form offers fewest technical difficulties in the

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are added. The suspension thus obtained is neutralised with 12.5 p. c. hydrochloric acid, or 15 p. c. caustic soda, red and blue litmus paper being used. If, for instance, 0.5 gramme of salvarsan are to be injected, this quantity is rubbed up with 0.45 gramme (8 drops) of caustic soda solution with constant stirring, and the mixture is tested with litmus paper. If it be acid it is neutralised with caustic soda; if it be alkaline it is neutralised with hydrochloric acid.

preparation, and is best suited for making ampoules containing the remedy ready for use. This form is also very well adapted for ambulatory practice. Kromayer recommends a 10 p. c. emulsion of unaltered salvarsan, i. e., of dioxidia-mido-arsenobenzol hydrochloride, in paraffin oil. It is said to keep well, and to cause no pain.

C. Schindler recommends the use of 25 p. c. iodipin for preparing the oily emulsion of salvarsan, for it does not decompose, it remains permanently sterile, is absorbed very readily, and never causes pain or infiltration as occurs when sesame oil is used. He obtained excellent results with a 40 p. c. emulsion of salvarsan oil prepared with iodipin and lanolin.

The treatment with salvarsan may be undertaken without hesitation in syphilitic patients who are strong and healthy in other respects, a single dose of 0.5 to 1 gramme being given. Michaelis reckons 0.01 gramme of salvarsan per kilogramme of patient's weight. Strong men are given 0.6 to 1 gramme, women 0.45 to 0.5 gramme. Weak persons are given 0.3 to 0.4 gramme, children 0.2 to 0.3 gramme, infants 0.02 to 0.1 gramme. Besides the intragluteal method of application, the intravenous injection (0.5 gramme), or the simultaneous intravenous and subcutaneous injection, must be fully considered. For intravenous injection the alkaline solution is probably preferable; for subcutaneous injection the paraffin emulsion. Of course these questions still await definite settlement\*). The same is true as to dosage; whether a single large dose should be used, and repeated later if need be in case of a relapse, or whether smaller amounts should be given at shorter intervals. The dose will depend, primarily, on the sensitiveness of the patient. Apparently, however, there is no need for undue care, for as yet no permanent ill-effects of any consequence have been observed with the Ehrlich-Hata remedy. The cases in which the new remedy has caused death directly have occurred in feeble persons or in those already greatly injured by paralysis; the transitory secondary effects mentioned by various authors form no contra-indication in any case in which the use of the Ehrlich-Hata treatment gives prospects of great benefit. The prepara-

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\*) See the official directions for use.

tion is contra-indicated in diseases of the heart and vessels, fœtid bronchitis, optic nerve disturbances, advanced degeneration of the central nervous system, non-syphilitic cachexia and idiosyncrasy for arsenic. In severe paralysis it should be used with great care, especially as there is at best little prospect of benefit in such cases.

The results to be expected with certainty from the use of the Ehrlich-Hata remedy in syphilis cannot be stated even now. Some authors report magical results, while others are more reserved. Further investigation is hence needed to determine whether the remedy merely acts on certain symptoms of syphilis, causing their rapid disappearance, or whether it effects an improvement in all the symptoms, or whether the condition of the patient plays a special rôle. Until the indications for "606" have been accurately established, we must expect successes to alternate with failures, as in the case of the action on the spirochætæ and the Wassermann reaction. Again, relapses will occur, not infrequently, in cured cases. The effective value of the remedy will not be placed in doubt thereby. We are fortunate to possess a remedy which is able to influence troublesome symptoms in most cases after a single injection, even though the relief might prove to be temporary. Certain conclusions as to this will not be available until ten years or more have elapsed.

Not only syphilis and paralysis, but also framboesia, malaria, recurrent fever, variola, psoriasis, lichen, leprosy, etc., have been treated, with varying results, with dioxidiamido-arsenobenzol.

The mode of action of the remedy also requires further investigation. We will merely point out that the action may, in the main, be comparable to that of the antitoxins. Possibly the preparation leads to the formation of antibodies in the organism. This view receives some confirmation from the experiments of Duhot and Raubitscheck. The abolition of the Wassermann reaction after the injection of "606", and the disappearance of the spirochætæ no doubt contribute to account for the specific action of the remedy.

In conclusion I append references to the most important publications on the Ehrlich-Hata preparation:

P. Ehrlich and S. Hata, *Die experimentelle Chemotherapie der Spirillosen* (Syphilis, Rückfallfieber, Hühnerspirillose, Framboesie). Berlin 1910. Published by Julius Springer.



- K. Alt, Das neueste Ehrlich-Hata-Präparat gegen Syphilis. Münchener medizinische Wochenschrift 1910, No. 11, p. 561; No. 34, p. 1774.
- J. Iversen, Über die Wirkung des neuen Arsenpräparates (606) Ehrlichs bei Rekurrens, Münchener medizinische Wochenschrift 1910, No. 15, p. 777. Über die Behandlung der Syphilis mit 606, Münchener medizinische Wochenschrift 1910, No. 33, p. 1723.
- Schreiber und Hoppe, Über die Behandlung der Syphilis mit 606, Münchener medizinische Wochenschrift 1910, No. 27, p. 1430. Die intravenöse Einspritzung des neuen Ehrlich-Hata-Präparates, Berliner klinische Wochenschrift 1910, No. 31, p. 1448.
- L. Michaelis, Über die Anwendung des Ehrlich-Hata'schen Syphilis-mittels in neutraler Suspension, Berliner klinische Wochenschrift 1910, No. 30, p. 1401. Die subkutane Anwendung des 606, Berliner klinische Wochenschrift 1910, No. 33, p. 1531. 110 Fälle von Syphilis, behandelt nach Ehrlich - Hata, Berliner klinische Wochenschrift 1910, No. 37, p. 1695.
- W. Wechselmann, Über die Behandlung der Syphilis mit Dioxydiamidoarsenobenzol, Berliner klinische Wochenschrift 1910, No. 27, p. 1263, Therapie der Gegenwart 1910, No. 7, p. 316. Über die Technik der Injektion des 606, Deutsche medizinische Wochenschrift 1910, No. 30, p. 1395. Beobachtungen an 503 mit Dioxydiamidoarsenobenzol behandelten Krankheitsfällen, Deutsche medizinische Wochenschrift 1910, No. 32, p. 1478. Über Reinjektionen von 606, Deutsche medizinische Wochenschrift 1910, No. 37, p. 1692. Besteck zur sterilen Injektion von 606, *ibid.* p. 1728.
- A. Neisser, Deutsche medizinische Wochenschrift 1910, No. 26, p. 1212.
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- Martius, Lokale Wirkungen des 606. Münchener medizinische Wochenschrift 1910, No. 52, p. 2768.
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### Santyl.

Santyl is reported on by G. Forconi and J. Sturdivant Read. Their trials with this remedy for gonorrhœa gave as good results as those previously obtained by a number of authors\*). Forconi, who used santyl in more than 50 cases, points out specially how well it is tolerated as compared with other balsams, while it never causes inflammation of the kidneys. Its action is also noteworthy, for the burning pain on micturition, the nocturnal erections and the pressure in the perineum subside under its use or disappear altogether. The author treated 6 cases of gonorrhœa and obtained a cure by the internal administration of santyl without other treatment. As a rule, however, the preparation is to be regarded merely as an auxiliary to local treatment, and it should be used accordingly. Sturdivant Read made use of this experience in prescribing it. In 2 p. c. only of the cases were gastric troubles observed after santyl treatment. This is the point where santyl proves itself superior to sandalwood oil, it produces the same action, but is accompanied by fewer secondary effects. The application and dosage of santyl have been described several times in these Reports\*\*).

### Sarton.

The fruit or seeds of the *Soja hispida* Mönch (*Dolichos Soja* L., or *Glycine Soja* Sieb.) is derived from a leguminous plant (*Phaseolaceæ*) cultivated in Eastern Asia (China and Japan). It has long been of interest in therapeutics, especially in the treatment of diabetes, by reason of the fact that it contains vegetable casein, sugar, starch and diastatic ferment, a fatty oil, cholesterin, lecithin, etc.\*\*\*).

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Forconi, Atti della reale academia di Fisio-critici in Siena 1909, No. 5. — Deutsche Medizinalzeitung 1910, p. 591.

Sturdivant Read, Long Island Medical Journal 1910, No. 2.

\*) See Merck's Reports 1905—1909.

\*\*) See Merck's Reports 1905—1909.

\*\*\*) See the following papers:

Meisel and Böcker, Rundschau für die Interessen der Pharmazie 1883, p. 414 (Leitmeritz).

Hanausek, Zeitschrift des österreichischen Apotheker-Vereins 1883, p. 475.

Haberlandt, Chemiker-Zeitung 1878, p. 357.



C. von Noorden and E. Lampé state that there are several sorts of soya seeds which vary greatly in quality and utility for dietetic purposes. The large amount of albumen contained in soya seeds (30 to 35 p. c.), and the small amount of starch and fermentable carbohydrates (about 6 p. c.), led these authors to try the use of soya seeds in diabetes. These are largely used in Japan as a vegetable. The seeds leave an unpleasant taste, and in their unaltered state have been shown by von Noorden to have a bad effect on the elimination of sugar in diabetes. A method had therefore to be found of removing the carbohydrates from the seeds, and of making them more palatable to Europeans. This has been done, and soya seeds are now issued in

Levallois, *Comptes rendus de l'académie des sciences* Vol. 93, p. 281.

Harz, *Zeitschrift des österreichischen Apotheker-Vereins* 1885, p. 40.

Stingl-Morawski, *Monatshefte für Chemie* 1886, p. 176, 1887, p. 82. — *Moniteur de la pharmacie belge* 1887, p. 82.

Trimble, *American Journal of Pharmacy* 1896, No. 6, 1897, No. 11.

Prinsen Geerligs, *Chemiker-Zeitung* 1896, p. 67.

Reber, *Der Fortschritt* (Genf) 1888, p. 246.

Lecerf, *Archives de médecine* 1888, p. 290. — *Pharmazeutische Zeitung* 1888, p. 501.

Pellet, *Union pharmaceutique* 1888, p. 355.

Blondel, *Pharmazeutische Zeitung* 1889, p. 118.

Stift, *Pharmazeutische Zentralhalle* 1889, p. 330.

Tahara-Kitao, *Revue internationale des falsifications* 1889, p. 159.

Belohubek, *Zeitschrift für das gesamte Brauwesen* 1889, p. 433.

Menudica, *Zeitschrift für Nahrungsmittel-Untersuchung und Hygiene* 1891, p. 216.

Kellner, *Chemiker-Zeitung* 1895, p. 97 and 120.

Osborne-Campbell, *Zeitschrift für angewandte Chemie* 1898, p. 636.

Williams-Langworthy, *Pharmazeutische Zeitung* 1897, p. 860.

Nikitin, *Russkij Wratsch* 1900, p. 674. — *Zeitschrift für Untersuchung der Nahrungs- und Genußmittel* 1901, p. 39.

Bloch, *Bulletin des sciences pharmacologiques* 1907, p. 536.

Bertrand, *Bulletin des sciences pharmacologiques* 1907, p. 65.

Schulze, *Zeitschrift für physiologische Chemie* 1907, Vol. 52, p. 404.

Yoshimura and Mitsuda, *Chemisches Zentralblatt* 1909, II, p. 644.

Friedenwald and Ruhrah, *American Journal of Medical Sciences* 1910, December.

von Noorden-Lampé, *Therapie der Gegenwart* 1910, No. 4.

the form of a powder (or of a paste) under the name of "sarton". This preparation contains neither starch nor sugar. It is used in the preparation of soups, to which butter, salt and spices are added. Its taste resembles that of soup obtained from ordinary white beans, and it is readily taken. The dish of soya seeds thus prepared forms an agreeable change in the diet of diabetic patients, while it has great nutritive value. Results in more than 100 diabetic patients show that in slight cases of diabetes the elimination of sugar is quite uninfluenced by sarton. In cases of moderate severity, in which a strict diet is just able to keep the urine free from sugar, and the slightest addition of starch flour gives rise to glycosuria, 80 to 100 grammes ( $2\frac{2}{3}$ — $3\frac{1}{3}$  oz) of sarton are equally well tolerated. In the still more advanced cases, soya soup as a rule causes no increase in the sugar when given in the quantities mentioned above. The use of sarton is not confined to the treatment of diabetes, it may be employed in any case in which vegetable albumen is preferred to animal albumen, e. g., in gout and in uric acid diathesis, in kidney diseases, and in many disturbances of the digestive organs. A secondary action of sarton which is appreciated by diabetics is a stimulation of the intestinal peristalsis without causing the formation of gas as occurs in most cases when fruits are taken. The chief value of sarton is attributed by von Noorden to the fact that it gives diabetic patients a new harmless food which agrees well and forms a welcome change.

### Scarlet red.

K. Wessely and H. Stoeber have proved experimentally that the subcutaneous injection of scarlet red oil produces, not only in rabbits but also in man, atypical epithelial growths. The action of scarlet red is rather less marked than usually observed on the rabbit's ear. Stoeber explains this observation on man by the anatomical character of this region (he injected the oil in the back of the foot) as well as by the absence of sebaceous glands and the small number of hairs.

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Wessely, Medizinische Klinik 1910, No. 14.

Stoeber, Münchener medizinische Wochenschrift 1910, No. 14

Gaudier, Lemaire, M. Strauss and K. Pein have reported on the treatment of wounds and ulcers with scarlet red ointment. The communications of these authors show that the drug has undoubtedly given good results. In using it care must be taken to avoid applying it to unclean, suppurating, œdematous or foul wounds; it should only be used for clean, flat wounds of a fresh red colour, otherwise its use is not successful. The method is very simple. The ointment (usually containing 8 p. c. of scarlet red) is spread upon wool or gauze to the thickness of the back of a knife, the wound is covered with it, and the dressing is not left for longer than 24 hours. If no inflammation is produced it may be renewed, while a dressing with paraffin ointment or with liquor aluminii subacetatis is applied alternately. The value of scarlet red treatment, according to Strauss, lies principally in its rapid action, a feature which many authors consider of great value, and also in the formation of tough epithelium which is of great value in all wounds in the neighbourhood of joints, for it prevents the wound from reopening. Burns are said to heal with great rapidity under this treatment. It also gives good results in ulcers of the leg, operation wounds, soft sores, syphilitic ulcers, and after incision in cellulitis and furuncles. The communications of the above named authors show that this is the case. In some cases of extensive moist eczema Strauss observed a surprisingly rapid growth of epithelium on the use of dilute scarlet red ointment. In loss of skin substance he observed very good epithelial growth in 2 cases, so that he was not obliged to carry out transplantation, which at first seemed necessary owing to the great extent of the lesion.

Scarlet red appears also to be finding an entry in veterinary practice. Successful results with it are reported by Köster and Picard. As in human medicine it is re-

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Gaudier, *Annales des maladies de l'oreille* 1910, April. — *Revue de thérapeutique* 1910, p. 671.

Lemaire, *Echo médical du Nord* 1910, 12<sup>th</sup> June.

Strauss, *Deutsche medizinische Wochenschrift* 1910, No. 19.

Pein, *Therapie der Gegenwart* 1910, No. 3.

Köster, *Zeitschrift für Veterinärkunde* 1910, No. 7.

Picard, *Revue générale de médecine vétérinaire* 1910, 15<sup>th</sup> October.

— *Berliner tierärztliche Wochenschrift* 1910, p. 942.



commended for wounds, ulcers, mallenders, bruised knees, etc.

### Scopolamine hydrobromide.

Further communications of great interest regarding the production of anæsthesia by means of scopolamine or scopolamine-morphine\*) have been published by C. Beer, Rinne, P. Sick, Otto, H. Torrance, Thomson, Kümmel, Clifford, U. Collins, Ruckert and J. Faust.

Beer, in his dissertation, enumerates the advantages and disadvantages of scopolamine-morphine anæsthesia. He then continues: A disadvantage of plain scopolamine-morphine anæsthesia is the incomplete relaxation of the muscles, which is especially necessary in laparotomies. Further, the dryness in the throat set up by this anæsthetic, and the thirst brought about by it are often disturbing factors; again, the tongue often falls back after the operation. The bad effect of morphine on the respiratory centre, and the recurrence of cyanosis have also been pointed out as disadvantages. Further objections are the difficulty as to dosage, the great rise in the frequency of the pulse, and the vaso-dilatation in the carotid region. As against these the following advantages have to be considered. Firstly, the anæsthesia commenced with scopolamine-morphine is far more humane, for the patients go to sleep in their usual bed, and they are spared the fear associated with the impending operation, and its reflex effect upon the heart. If veronal be given the night before the operation, a quiet night is passed and the heart consequently performs its functions

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\*) See Merck's Reports 1902—1909.

Beer, Dissertation Freiburg i. Br. 1910.

Rinne, Deutsche medizinische Wochenschrift 1910, No. 3, p. 110.

Sick, Deutsche medizinische Wochenschrift 1910, No. 9, p. 406.

Otto, Medizinische Klinik 1910, No. 10, p. 380.

Thomson, Edinburgh Medical Journal 1909, December. — Deutsche Medizinal-Zeitung 1910, No. 16, p. 276.

Kümmel, Klinische Monatshefte für Augenheilkunde 1910, No. 4.

Collins, Journal of Obstetrics and Gynaecology (London) 1910, No. 6, p. 549. — Journal of the American Medical Association 1910, p. 1051.

Ruckert, Zeitschrift für Geburtshilfe und Gynäkologie Vol. 66, No. 2.

Faust, Deutsche medizinische Wochenschrift 1910, No. 11, p. 508.

better. Another circumstance of importance is the fact that the patients continue to sleep after the operation. The vomiting is prevented, which may be a source of danger, especially in laparotomies when the tension on the sutures gives rise to pain in the wound. If vomiting is not entirely prevented at any rate it is postponed for several hours. The salivation which is a disturbing sequel, especially after ether, is considerably diminished by scopolamine, while post-operative bronchitis and broncho-pneumonia occur less frequently. A fact which strongly favours the use of scopolamine-morphine is that the consumption of ether or chloroform is far smaller, so that even in severe valvular affections, chloroform anæsthesia, which would otherwise be dangerous may be adopted.

P. Sick has been led by his experience with mixed anæsthesia to the result that the excellent action of scopolamine in combination with inhalation anæsthesia may be increased by giving at least 2 doses, adjusted to each individual case, whereby the need to use chloroform in dangerous quantity is entirely eliminated, and ether, the amount of which is reduced to a third of the usual quantity, may be used in almost all cases without fear of irritating the lungs. The hypnotic action may be produced by scopolamine alone, the dose of which may be increased without danger, while the dose of morphine should be kept as low as possible, and a single dose only should be given with the last injection. Sick considers the danger of the Schneiderlin-Korff method of anæsthesia to be due not to the scopolamine, but solely to the morphine. When used in correct proportions the combined anæsthetic should be given the first place, for its indications are very wide and its use (even in unpractised hands) is free from danger. The author utters a warning against general scopolamine-morphine anæsthesia. Otto comes to similar conclusions. He considers the specific action of mixed anæsthesia to be due to the use of several anæsthetics in the smallest possible doses, enabling the desired effect to be produced without poisoning. After administering 0.5 to 1 gramme ( $7\frac{1}{2}$ —15 grains) of veronal the night before the operation, and 0.0003 to 0.0006 gramme ( $\frac{1}{200}$ — $\frac{1}{100}$  grain) of scopolamine hydrobromide with a single dose of morphine, a sufficient degree of "dawning-sleep" is produced, invariably in women though

not always in men. The dose of morphine should not be greater than 0.01 gramme ( $\frac{1}{8}$  grain), and larger doses should not be given. The dose of scopolamine, however, may be increased without danger (to 0.0009 gramme). Similar conclusions as those of Sick and Otto are come to by Ruckert, Collins, Thomson, and Kümmel as to the value of scopolamine-morphine for inhalation anæsthesia.

The fact that excessive doses, especially in feeble persons, may be dangerous, is brought out by a communication by Rinne. In one case he gave a larger dose of scopolamine (0.0012 gramme scopolamine and 0.03 gramme morphine) in three portions, within 3 hours before the operation (without inhalation anæsthesia). In another case he gave the same dose within two and a half hours (with ether inhalation). In both cases the treatment ended fatally. The author attributes the disastrous termination not to the anæsthesia alone, but to severe changes in the vascular system which were shown at the post-mortem examination. Faust observed transitory paralysis of respiration after the use of the same large dose. He attributes it to the scopolamine, but this cannot be accepted without further enquiry, considering the results published by Sick and Otto.

In opposition to the criticism of Beer in pointing out the disadvantages of the use of scopolamine, Kretz recognises only one disadvantage of scopolamine-morphine "dawning sleep", which is that scopolamine produces a feeling of great thirst. It is said that this can be readily diminished by washing out the mouth. Kretz recognises the advantages of the method as described by the above named authors. As to the increase in pulse rate after scopolamine, described by various observers, Kretz carried out experiments which showed that a rise of pulse rate is only observed in a very small proportion of the cases treated, and must then be attributed to a rise of temperature. B. Bosse and W. Eliasberg prescribed scopolamine and morphine in the same way as previously used by Cremer for the

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Kretz, Medizinische Klinik 1910, No. 40, p. 1568.

Bosse-Eliasberg, Sammlung klinischer Vorträge (Volkmanns) 1910, No. 599/601, Gynäkologie No. 215/217.

Cremer, Medizinische Klinik 1910, No. 28, p. 1092. See also Ärztliche Vierteljahrsrundschau 1906, II, p. 27 and Heilmitelrevue 1906, No. 5, p. 67.



“dawning sleep” which has become so popular in operations and confinements:

Rp. Scopolamin. hydrobrom. Merck 0.003 gramme ( $\frac{1}{20}$  grain)  
d. ad vitrum sterilisatum  
and

Rp. Morph. hydrochlor. 0.1 „ ( $\frac{1}{2}$  grains)  
d. ad vitrum sterilisatum

Sig.: To be used by the physician. (Dawning sleep.)

Bosse says in this connection: “The most important point is still, as Cremer pointed out, to use Merck’s scopolamine in all cases, for it is free from optically inactive constituents. Because of the labile properties of the alkaloid, neither tablets nor Riedel’s scopomorphine solution should be used; the solution should be prepared fresh for use each time.” The paper published by the two authors on the use of scopolamine-morphine describes mixed anæsthesia in all its bearings, including the indications, contra-indications, dosage, methods of application, and full details. It contains too much to enable it to be reproduced in a brief form, hence those interested should refer to the original paper. With regard to the use of scopolamine “dawning sleep”, it should be added that M. Salzberger, in a paper on this subject from the Women’s Hospital of Freiburg, states that scopolamine, when used in correct doses, does not endanger the life, the health, or the development of the child.

Bürgi showed in an interesting paper that two anæsthetics introduced simultaneously or shortly after one another had a more powerful action, as a rule, than would be expected from the sum of the individual effects. E. Hauckold then studied the effect of scopolamine on the action of urethane and ascertained by experiments that scopolamine, which does not produce anæsthesia in rabbits by itself, has a considerable effect in enhancing the anæsthetic properties of urethane. Small quantities of urethane which would not by themselves produce anæsthesia showed a narcotic action by means of a minimal dose of scopolamine. Hauckold found scopolamine to have a similar action in combination with morphine.

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Salzberger, Dissertation Freiburg i. B. 1910.

Bürgi, Korrespondenzblatt für Schweizer Ärzte 1909.

Hauckold, Zeitschrift für experimentelle Pathologie und Therapie 1910, Vol. 7, No. 3, p. 743.

A. Luxardo used scopolamine to advantage instead of atropine in the replacement of inguinal herniæ. The dosage must be adjusted to suit the case. The author places an ice bag on the affected region; he injects 0.0005 gramme ( $\frac{1}{120}$  grain) of scopolamine hydrobromide Merck, and then 0.005 gramme ( $\frac{1}{12}$  grain) morphine hydrochloride. As much as 0.001 gramme ( $\frac{1}{64}$  grain) of scopolamine may be used, but if no success is obtained with this an operation must be undertaken.

M. Neu made trials to ascertain whether the absolutely harmless anæsthesia produced by laughing gas (nitrous oxide and oxygen) might not be enhanced by the previous use of scopolamine-morphine. The results obtained by experiments on animals show that this is in fact the case. If this is found to be confirmed in man, it is to be hoped that this combination may give us a method of producing anæsthesia which does no harm to the circulation and respiration, and has no after effects.

Scopolamine has been found, by H. V. Riewel, to be of good service in the treatment of morphinism, and especially alcoholism. The author directs that the remedy be given for about a week internally in doses of 0.0005 to 0.001 gramme ( $\frac{1}{120}$ — $\frac{1}{64}$  grain) in combination with small doses of atropine and strychnine several times a day. After this the preparation is given for 2 to 3 days subcutaneously in sufficient quantity to produce slight delirium. With this treatment it is said that the desire for alcohol and morphine is abolished.

### **Semen Cucurbitæ Pepo.**

Pumpkin seeds have always enjoyed a popular reputation as a remedy for tapeworms. They have therefore been worked up into special preparations. The active constituent of the drug has so far not been recognised. Hence the investigations of F. B. Power and A. H. Salway are

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Luxardo, *Gazzetta degli ospedali e delle cliniche* 1910, 9<sup>th</sup> June.  
Neu, *Münchener medizinische Wochenschrift* 1910, No. 35, p. 1873.  
Riewel, *Monthly Cyclopaedia and Medical Bulletin Philadelphia* 1909, October. — *Therapeutische Monatshefte* 1910, No. 5, p. 271.

Power-Salway-Dale, *Journal of the American Chemical Society* 1910, p. 346.

interesting. They found the oil expressed from the seeds to consist of a mixture of 45 p. c. of glycerides of linoleic acid, 25 p. c. of oleic acid, and 30 p. c. of palmitic and stearic acids. The part which cannot be saponified contains a phytosterol melting at 162 to 163° C. From the compressed mass they were able to extract 8.7 p. c. of this oil by means of alcohol; they also extracted soluble albuminous substances, sugar, traces of salicylic acid and 0.5 p. c. of resin. From the latter they were able to isolate a monocarboxylic acid,  $C_{25}H_{51}O.COOH$ , which melts at 99° C. To ascertain whether the oil thus obtained or the resin is responsible for the action of the seeds, H. H. Dale made experiments which yielded the surprising result that it was found that neither of these substances had an anthelmintic action. The same result was obtained in testing the whole seed. Hence the therapeutic value of pumpkin seeds, which have not yet become recognised medically as a remedy for tapeworms, is very questionable.

### Sera and Antigens \*).

#### Antithyroidin.

The communications in the past year by von Devic and Gardère, G. Righetti, C. Panafiel, J. R. Gilmour, Baugh and L. Noellner afford further evidence as to the utility of this well recognised remedy for the treatment of Graves's disease and of its effects. Devic and Gardère report on a severe case of Graves's disease in which the serum treatment sufficed to produce a complete cure. The authors used the preparation in the form of subcutaneous injections with suitable diet and the administration of arsenic. For 10 days 1 c. c. of serum was injected every other day, then 1 c.c. daily for a further period of 10 days, and then 2 c.c. daily for a third period

\*) These articles continue and complete the series of articles in last year's Reports on "Serum Therapy and Bacterio-Therapeutic Preparations".

Devic-Gardère, *Lyon médical* 1910, No. 37 and 38.

Righetti, *Giornale internazionale delle scienze mediche* 1910.

Panafiel, *Revista syniatica* 1910, No. 5.

Gilmour, *Journal of Mental Sciences* 1909, October.

Baugh, *ibid.*

Noellner, communicated in a letter.



of 10 days. After an interval of 10 days the series of injections was carried out anew. Thus the patient received 70 c. c. of antithyroidin in two series. With this treatment the patient gained in weight, the circumference of the neck diminished by 2 cm., the tachycardia diminished, and the insomnia disappeared. On continuing the treatment the improvement continued, menstruation came on again, the pulse became regular and good sleep was obtained. After rather less than a year and a half's treatment the patient was in a good state of health. This very good result leads the author to recommend thyroid serum in severe cases of Graves's disease running a rapid course. In such cases, however, the injections must be continued perseveringly for a number of months. A similar report is given by Gilmour, Baugh and Panafiel, who gave antithyroidin internally in doses of about 5 c. c. a day. The improvement in the various symptoms after a short course of treatment was transitory; long-continued treatment was necessary to produce a permanent effect.

Noellner used antithyroidin treatment in about 10 cases of goitre. In one only of these cases the goitre became softer, though not smaller, while in all other cases there was a material reduction in the size of the goitre, even when it did not disappear altogether. Two cases are particularly remarkable, for in these there was danger of suffocation which had brought up the question of operative interference. The author decided to use antithyroidin. In one of the cases the goitre diminished appreciably, although the diminution was slight. The shortness of breath, however, which had been present for a long time, left off, although previously dyspnoea had occurred every time the patient bent forward. In the case of another patient with a goitre the size of a fist, this subsided to the size of a small apple, and hung on the neck as a loosely filled sac. The considerable dyspnoea subsided after not more than 30 grammes of antithyroidin had been taken. In these two cases 50 grammes of the preparation were used in all, in doses rising from 4 drops 3 times a day to 10 drops 3 times a day. The earliest case treated by Noellner was two years ago. The result obtained with antithyroidin was a permanent one in this case, while in cases treated earlier with iodine ointment and electricity the improvement was followed by a relapse\*).

\*) See Merck's Reports 1909, p. 24—32.

### **Anthrax serum.**

The results of the serum treatment of anthrax in veterinary practice have awakened interest in the specific treatment of anthrax in human medicine to such an extent that Sobernheim's anthrax serum has been used on an increasing scale as an addition to the older forms of medicinal treatment. Recently Koelsch has again drawn attention to the value of this serum. It is best given intravenously in doses of 10 c. c., repeated several times. The most conservative local treatment should be used with it. Beyer used pyocyanase for the local treatment. In the two cases reported by him the infection occurred in a tannery. One patient had a pustule on the right cheek. He was given two intravenous injections, and the pustule was treated locally with pyocyanase. The case ran an afebrile course and ended in recovery, so that there was practically no scar to be seen. In the other case there was fever and oedema extending to the eyelids. The treatment consisted of 3 injections of serum, amounting altogether to 50 c. c., and moist dressings with pyocyanase. On the fourth day a complication occurred in the form of erysipelas starting from the primary lesion. The pustule healed, but a scar was left which necessitated a plastic operation. The serum injections should be commenced as soon as anthrax is diagnosed. It is therefore advisable, in vocations in which anthrax infection is known by experience to be liable to occur, that serum be kept at hand so that too much time may not be lost in procuring it.

### **Arthigon.**

C. Bruck states that the vaccine treatment of gonorrhœa, or of its complications, gonorrhœal epididymitis, is founded on a sufficient theoretical basis to justify a thorough trial in this direction\*). A suitable preparation for this purpose is found in arthigon, a gonococcal vaccine which is said by C. Schindler to contain 20 000 000 killed gonococci in each

Koelsch, Münchener medizinische Wochenschrift 1910, No. 31, p. 1641.

Beyer, Münchener medizinische Wochenschrift 1910, No. 7, p. 385.

Bruck, Deutsche medizinische Wochenschrift 1909, No. 11, p. 470.

— Medizinische Klinik 1910, No. 21, p. 811.

\*) See Sakubane und Yasuki, Mitteilungen der medizinischen Gesellschaft in Osaka 1909, Vol. 8, No. 7.

Schindler, Berliner klinische Wochenschrift 1910, No. 31, p. 1446.

c. c. The manner in which active immunisation reacts on the gonorrhœal process is shown by Bruck to be incapable of definite explanation. It is possible that the antibodies formed by the immunisation, and demonstrable by experiment, have an effect on the gonococci. Bruck considers it more probable, however, that the vaccines act in the same manner as tuberculin by producing a specific reaction on the gonorrhœal tissues favourable to a cure. In fact the author has been able to show that the vaccine treatment has led to exceedingly favourable results in two complications of gonorrhœa, arthritis and epididymitis. In his experience the pain soon subsides, though the first injection is frequently followed by increased pain (local reaction?)\*). Absorption follows rapidly, the formation of nodes does not occur, or occurs in a much reduced degree. The earlier the treatment is commenced the better are the results. Even in chronic cases of epididymitis, however, in which hard infiltration was present, the author frequently obtained improvement. Scar tissue, it is true, will be more readily influenced by a remedy which softens it, such as fibrolysin, and in no case are wonders to be expected of vaccine treatment. Bruck points out specially that he has never observed a relapse or the extension of the disease to healthy parts. Neither is any injury to be anticipated from treatment. It is contra-indicated in febrile cases, for it produces a specific fever on its own account. In such cases the temperature must first be brought back to normal by other means. The specific treatment is of no use in old nodes.

The injections of arthigon are made with a sterile Pravaz syringe into the gluteal muscles. With regard to dosage, sufficiently large doses must be given to produce a pronounced reaction\*\*), apparent by a rise of temperature of at least

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\*) Also observed by C. Jarvis (*Presse médicale* 1910, p. 161) and by Sowinski (*Russkij Wratsch* 1910, p. 700) on treatment with gonococcus vaccine.

\*\*) Jamieson-Torreon advises that in acute cases of gonorrhœa small doses (5—10 million gonococci) be used, while in chronic cases large doses (commencing with 50 million) should be used. (*Therapeutic Gazette* 1910, May). In Sowinski's opinion only the chronic and sub-chronic cases are suitable for vaccine treatment. Jarvis considers frequently repeated small doses more efficacious than large doses applied at longer intervals.



10, lasting a day. We should begin with 0.5 c. c. of vaccine. If the temperature rises we must wait 3 to 4 days, when the dose should be repeated. If the reaction is but slight after waiting 3 to 4 days, 1 c. c. should be injected. If no rise follows this injection, a larger dose is injected 2 days later. In this way the author gave 0.5—1.0—1.5—2.0 c. c. He never used larger doses than these, and he never gave more than 5 or 6 injections in succession. A scheme of universal applicability cannot be given, for, as in all cases of active immunisation, regard must be had to the temperature curve in each case.

Schindler tried not only arthigon, but also Reiter's vaccine which contains 5 000 000 killed gonococci in each c. c. He found that immunisation with arthigon was more rapid and more intense. The communications so far published by the author show that in epididymitis and diseases of the appendages, although the cases he has treated have been few, both vaccines afforded curative results that were so rapid as to convince him that the specific treatment of these diseases and of gonorrhœal arthritis gives promise of successful application.

### **Cholera serum.**

A. T. Salimbeni reports on his results obtained during the cholera epidemic of 1908 with his cholera serum prepared in the Pasteur Institute in Paris. It was obtained from horses by the method of Roux and Metschnikoff, the horses having been previously treated with soluble cholera toxins. Salimbeni states that the serum is so rich in antitoxins that it is able to neutralise double its amount of cholera toxin. As a rule it was mixed with normal saline solution, and injected subcutaneously in quantities of 100 to 150 c. c. It gave particularly good results in severe cases, provided it were used early enough. It was of no use, however, when injected in too far advanced a stage of the disease. The practical conclusion may be derived at once that the serum should be prescribed as early as possible. Its action is then apparent in the favourable course of the illness; the vomiting ceases, the respiratory troubles, cramps and diarrhœa subside, and the fæces acquire a normal colour. Salimbeni had a death rate

of 47 p. c. in very severe cases treated with serum, of 10 p. c. in severe cases, and no deaths in cases of moderate severity and in slight cases. No disadvantage of the serum injections was observed by the author in any case. These results led him to regard the use of serum in the treatment of cholera as a means that cannot be valued too highly.

### **Gonococcus serum.**

The specific treatment of gonorrhœa has begun slowly to find recognition since reliable preparations have appeared on the market. Thus W. Schiele and F. Dörbeck report on a case of gonorrhœal endocarditis in which great benefit was obtained by subcutaneous injections of antigonococcus serum. The case was that of a young patient with acute anterior and posterior gonococcal urethritis with severe complications. The authors used the serum in three series of 3 ampoules (each containing 2 c. c.). The result was surprising, for immediately after the first injection the temperature, after rising for a brief time to 39° C., fell to normal on the following day, and did not rise again. On the local processes, however, the serum had no effect, and it was necessary to inject potassium permanganate solution and to give internal doses of salol, santyl, urotropine, etc., for their relief. The prompt fall of temperature is ascribed by the authors to the use of serum, as well as the subsidence of the general symptoms and of the acute inflammation of the heart.

### **Meningococcus serum.**

It has been observed with all sera, and the serum for cerebro-spinal meningitis is no exception, that a success is only obtained if it is used sufficiently early. This fact is supported by the results of C. E. Bloch's investigations. Patients in a somnolent, unconscious or moribund state when subjected to specific treatment, show practically no tendency to recover. If the serum treatment be commenced early, however, it is of excellent service. In the author's experience this is only the case when the serum is

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Schiele-Dörbeck, Petersburgers medizinische Wochenschrift 1910, No. 45, p. 605.

Bloch, Hospitalstidende 1909, No. 42. — Deutsche Medicalzeitung 1910, No. 19.

injected in large doses intraspinally after lumbar puncture. Subcutaneous or intramuscular injections appear to be of no appreciable benefit. In children 20 c. c. should be injected, in adults at least 40 c. c. These doses should, as a rule, be repeated every other day and continued until a definite effect is obtained. Although as a rule more serum may be injected than the amount of cerebro-spinal fluid removed it is advisable to prevent a rise of intracranial pressure by injecting rather less serum. There is no objection, even in children, to withdrawing 30 to 40 c. c. of cerebro-spinal fluid, at least this is the result of Bloch's experience. In favourable cases all the symptoms subside very soon after the injection. Even after the first injection the author observed the subsidence of severe hyperæsthesia, opisthotonos and headache; they disappeared as at a stroke. Patients who had no rest for days fell into a calm sleep. Further, the duration of the illness was considerably shortened, so that in severe cases the acute stage had passed 7 to 8 days after the first injection. Moreover, the patients remained free from complications such as hydrocephalus with continued vomiting and cramps, bedsores and extreme wasting. These results cannot, in the author's opinion, be attributed to the lumbar puncture, for the relief obtained by this is usually of short duration and cannot be compared with the action observed after the injection of serum. In the case described, moreover, the intracranial pressure was not reduced, for just as much serum, if not more, was introduced as the cerebro-spinal fluid which was withdrawn. Compared with earlier results of serum treatment, Bloch's results justify the assumption that meningococcus serum is a valuable agent in the treatment of cerebro-spinal meningitis\*). A similar conclusion is arrived at by F. Göppert in an interesting publication on the preparation of meningococcus serum, its active substances, the details of its application, and its curative effects.

### **Streptococcus serum.**

A case of articular rheumatism in which a brilliant result was obtained by Menzer's streptococcus serum has been described by H. Ratzeburg. The case was that of a

\*) See Merck's Reports 1909.

Göppert, *Therapeutische Monatshefte* 1910, No. 9.

Ratzeburg, *Therapie der Gegenwart* 1910, No. 3, p. 107.



man approaching 50 years of age who had suffered from articular rheumatism four years previously, and had had frequent severe relapses in the meantime. The last relapse was especially obstinate, and resisted all treatment. 23 c. c. of the serum were therefore injected. The disease thereupon gradually subsided, and no further trouble occurred. As the result of this successful case the author gives the indications and method of using the serum. In the first place he states that in acute and sub-acute cases of articular rheumatism an attempt should first be made with salicylic treatment, and in chronic articular rheumatism a trial should be made with the older recognised remedies such as hot air baths, vapour baths, sand baths and massage. If it appears that the usual medicinal, mechanical and hydropathic measures are of no value, use of the serum should be made. For this purpose the author advises the careful disinfection of the physician's hands, and of the seat of the injection, the outer side of the thigh. A sterile Pravaz syringe should be used with 2 cannulæ (holding 2 c. c.) and the serum should be injected subcutaneously. One cannula is left in place while the other is used to refill the syringe. The amount to be injected must be determined by the constitution of the patient. In children 2 c. c. are sufficient for a single dose, in adults as a rule 5 c. c., but as much as 10 c. c. may be injected. If a total amount of 30 c. c. has been used it is advisable to allow an interval of at least 1 to 2 weeks. In conjunction with the earlier reports of successful treatment with serum, the favourable effect of Menzer's streptococcus serum reported by Ratzeburg affords a proof that in apparently hopeless cases of polyarthritis surprisingly good and permanently successful results may be obtained with the serum.

K. Ungar used Menzer's streptococcus serum in a case of very severe sepsis following abortion. He obtained a very decisive result; the patient came under treatment with a temperature of 40.6° C., intense rigors, a small, frequent pulse of low tension, bronchitic râles in the lungs, definite enlargement of the spleen, purulent vaginal discharge, and meteorism. The bacteriological examination showed streptococcic sepsis. Saline infusions, digitalis and alcohol led to

an improvement in the pulse and in the patient's strength, but the improvement was counteracted by the rigors. This treatment was then assisted by the injection of 15 c. c. of serum, with the result that the temperature fell at once, the rigors left off entirely, and the patient improved visibly. The symptoms came on again after several days, and 10 c. c. was injected intravenously. Convalescence followed after this injection.

### **Suptol Burow.**

In a communication on the results of inoculation with this vaccine, which has already been mentioned several times in these Reports\*), Tillmann mentions his results in this direction. They speak greatly in favour of suptol. To prove the efficacy of the remedy, he left 40 young pigs without inoculation in one stable. Of these 12 died in the first four weeks, 3 after 4 months, while six were permanently crippled. Of 65 inoculated animals not one was lost. An equally good result was obtained by the author in more than 100 young pigs. If the results in the animals treated and those not treated be compared, it is impossible to deny the definite curative value of suptol. Tillmann therefore considers suptol to be the most efficacious remedy known at present for the treatment of swine fever. This view may be adopted without hesitation after studying the comprehensive review written by Burow on the results obtained with suptol. Those interested should refer to this communication.

### **Tuberculin.**

With regard to the statements in my last Reports (1909) on tuberculol and tuberculin, there is an interesting paper by K. Siegesmund in which he examines the strength of the various commercial tuberculins. Siegesmund used the usual method of Koch, as carried out in the Institute for Experimental Therapeutics of Frankfort o/M., and tested tuberculin - Dohna, tuberculin - Béranek, and Berne tuberculin, and also tuberculol-Landmann. As a prototype he took

\*) See Merck's Reports 1907, 1908 and 1909.

Tillmann, Berliner tierärztliche Wochenschrift 1910, No. 39.

Burow, Berliner tierärztliche Wochenschrift 1910, No. 26.

Siegesmund, Zeitschrift für Hygiene und Infektionskrankheiten 1910, Vol. 66. — Berliner tierärztliche Wochenschrift 1910, No. 43.

the standard tuberculin of the Institute, against which all kinds of tuberculin officially used in Germany are standardised. In his comparative trials he found tuberculin-Béraneck to be the weakest. It contained at least 3.3 times less tuberculous toxin than the standard tuberculin. With the Berne tuberculin the lethal action was shown to be one-third to one half weaker than that of the standard tuberculin. Tuberculin-Dohna was found to be as strong as the standard tuberculin, but the author describes it as untrustworthy, for in two series of experiments its action was found to be irregular. Tuberculol B\*), the extract from tubercle bacilli, was found of equal strength with the standard tuberculin. Tuberculin A was decidedly stronger in three tests; in one it was 3.5 times stronger. Bovotuberculol, a 50 p. c. solution of tuberculol D which contains the extracts and secretion from the tubercle bacilli of cattle, was found to be 2.5 times stronger than standard tuberculin. Since bovyotuberculol is a 50 p. c. solution of tuberculol D it is obvious that its action is 5 times stronger than that of the standard tuberculin. Tuberculol C, the secretion from human tubercle bacilli, contains so much specific tuberculous toxin that it considerably surpasses all other preparations; it is about 10 times as strong as the standard tuberculin, and 30 times stronger than tuberculin-Béraneck.

As to the value of tuberculin in the treatment of pulmonary tuberculosis, an enquiry started by the "Medizinische Klinik" (a weekly journal for practitioners) has elicited contributions from F. Kraus, N. Ortner, H. Eichhorst, Hirsch, v. Leube, Moritz, F. Müller, Soltmann and Heubner. With the exception of Eichhorst, all the authors express an opinion which is favourable on the whole to tuberculin treatment, and in some cases very favourable. Those interested should refer to the original communications, as they cannot be referred to in a brief abstract.

The fact should be noted that a new tuberculin preparation has recently been issued that is free from albumen; it is called "endotin". Its use and indications are the same as

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\*) Tuberkulol A, B, C and D see Merck's Reports 1909, p. 79.

Kraus, Ortner, Eichhorst, Hirsch, *Medizinische Klinik* 1910, No. 1.  
v. Leube, Moritz, Müller, Soltmann, Heubner, *Medizinische Klinik* 1910, No. 5.



for other commercial tuberculins, but it is said to be distinguished by its high degree of purity. Reports on it have been published by Gabrilowitsch, Hirschberg, Neumann and Gordon. G. Jochmann and B. Möllers regard endotin as very poor in specific active substances, though it is certainly not weak in the isolated specific substance of old tuberculin. For this reason it is not superior to other tuberculin preparations, in fact it is distinctly inferior.

### **Typhoid serum.**

A method of preparing active typhoid antitoxins is described in a paper by A. L. Garbat and F. Meyer. They arrived at the result that the typhoid bacillus contains two different toxins, the toxin of the bacterial wall, which appears not to exert its activity until it reaches the living organism, and the internal nuclear toxin, which is set free when the surrounding cell wall is dissolved. Both constituents act as antigens, and produce antibodies which differ quantitatively. While the injection of the whole bacteria produces antibodies which have agglutinating complement-binding and bacteriolytic properties, injections of endotoxin produce principally bacteriotropic and moderately curative sera. A good serum does not fulfil its purpose, however, unless it possesses antibodies for both antigens, and this may be obtained by mixing the two types of serum. These mixed sera form a new kind of specific serum. It is possible that a better result will be obtained in the treatment of typhoid when they are used, than has been obtained with the curative sera that have been prepared up to the present. Of course this question must be definitely settled by clinical investigation\*).

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Gabrilowitsch, *Tuberkulosis* 1909, No. 11.

Hirschberg, *Petersburger medizinische Wochenschrift* 1910, No. 9.  
Neumann, *Brauers Beiträge zur Klinik der Tuberkulose* 1910, No. 1.

Gordon, *Deutsche medizinische Wochenschrift* 1910, No. 38.

Jochmann-Möllers, *Deutsche medizinische Wochenschrift* 1910, No. 46.

Garbat-Meyer, *Zeitschrift für experimentelle Pathologie und Therapie* 1910, Vol. 8, No. 1, p. 1.

\*) See the article Typhoid Serum in Merck's Reports, 1909.

**Wassermann's Syphilis Test as modified by von Dungern.**

Since its introduction into practice, Wassermann's syphilis reaction\*) has been variously judged as to its value and its significance, but it appears that the opponents of this method are decreasing in number. Quite recently F. Blumenthal in an extensive experimental work illustrated Wassermann's test in all branches of its application, and has ascertained that it is an undeniable advance in the diagnosis of syphilis. The principal conclusions of his investigations are as follows: Wassermann's reaction is present, as a rule, (in the initial stages of the disease) in the fifth to the sixth week, and increases from this time, provided successful treatment be not adopted in the meantime. The author obtained the reaction in the primary stage in 62 p. c. of his cases. In the other stages he found the test to be positive in about 95 p. c. of the cases. Even in cases in which syphilis is undoubtedly present a negative result may occur. Hence, even when the result is negative the test must be repeated at intervals, otherwise mistakes may occur. A strongly positive result of the test shows, with almost 100 p. c. probability, that syphilitic infection is present, unless tropical frambœsia, malaria, scarlet fever or leprosy are possible alternatives in the differential diagnosis. Again, a negative result gives us a 95 p. c. probability that a doubtful affection is not syphilitic. By mercury treatment a positive test is frequently changed to a negative one, but may become positive again after a time. The fact should be noted that cases in the latent stage which do not react may give a positive test at first under mercury treatment. The author's experience shows, further, that the result is of no significance on the prognosis during the years which immediately follow the infection. In later years a negative test must be used with care as a prognostic sign, for the test may become positive again at any time. Hence a negative result obtained by treatment cannot be regarded as proof of a cure without further investigation, for the spirochætæ may be in a resting state, and thus produce no signs of disease. The test cannot be used to afford an indication whether a syphilitic subject is infectious. The Wasser-

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\*) See Merck's Reports 1908, p. 308.

Blumenthal, Dermatologische Zeitschrift 1910, No. 1 and 2.

mann test therefore affords the only means of ascertaining the presence of latent syphilis among persons infected with syphilis, and of ascertaining whether a cure is to be obtained by treatment.

Others have recognised the importance of Wassermann's syphilis test, and if it has not yet become the general property of medical men, the reason is that the method described by Wassermann was tedious and difficult, and required a suitably equipped laboratory, and sufficient knowledge of serology. Noguchi therefore worked at simplifying Wassermann's reaction. A simple manipulation which can be carried out by any medical man in his consulting room has now been obtained by E. von Dungern and Hirschfeld. To apply the Wassermann test we require a normal saline solution and also

1. Patient's serum,
2. Organ extract,
3. Guinea pig's serum (complement),
4. A hæmolytic system, consisting of blood corpuscles of any kind, and a hæmolytic antibody to these blood corpuscles (amboceptor).

The simplification introduced by Dungern's method enables the test to be carried out without previous knowledge and without a laboratory. It consists in using, in place of animal blood corpuscles, those of the patient, and in using other reagents ready titrated, in a stable form.

To prepare the normal saline solution 0.8 gramme of sodium chloride (I issue sodium chloride tablets containing 0.8 gramme for this purpose) are dissolved in 100 c. c. of ordinary water.

The guinea pig's serum is dried upon the accompanying "complement paper". The "organ extract" is in alcoholic solution. The tube must be kept well sealed, so that it does not gain in concentration by the evaporation of the alcohol. The bottle labelled "amboceptor" contains a weighed quantity of dried serum adjusted to human blood (goat's serum which dissolves human blood). A glass contains enough for 5 tests. 2.2 c. c. of normal saline solution are placed in the

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v. Dungern, *Münchener medizinische Wochenschrift* 1910, No. 10.

v. Dungern-Hirschfeld, *Münchener medizinische Wochenschrift* 1910, No. 21. — *British Columbia Pharmaceutical Record* 1910, No. 6, p. 148.



glass (8.8 c. c. in a glass for 20 test), and the powder is dissolved in it by shaking. From the patient's finger about 10 drops of blood are then collected in a watch glass, and are stirred up with a wooden match for a few minutes until fibrin is seen to adhere to the match. The defibrinated blood thus obtained contains the patient's serum (see No. 1 above), and the blood corpuscles necessary for the hæmolytic system (see No. 4 above). The test is now carried out as follows:

1. Two test tubes are taken of 10 mm. diameter. In the bottom of one of them 0.05 c. c. of the alcoholic "organ extract" is placed by means of a pipette. The test tube and pipette must previously have been rinsed with alcohol and thoroughly dried.
2. The part of the pipette that has been wetted with alcohol is washed with water and saline solution, and 2 c. c. of saline solution are placed in each of the test tubes.
3. Into each of the test tubes are placed 2 strips of complement paper which must be completely covered by the fluid. If this is not the case the test tubes are too wide.
4. Into each tube is introduced 0.1 c. c. of the patient's defibrinated blood.
5. The tubes are left standing at ordinary temperature for at least one hour and are shaken from time to time.
6. Into each tube is placed 0.2 c. c. of amboceptor solution. The tubes are shaken. After 10 to 15 minutes they are again shaken.

In the tube which contains no organ extract (control), solution of the blood takes place after a short time, the fluid assumes a transparent red (laky) colour.

In the tube to which organ extract has been added, if the test is negative, solution takes place at once, or very soon. When the test is positive, the blood corpuscles in the tube containing organ extract collect into a ball (agglutination), but no solution of red blood corpuscles occurs. After about 30 minutes the supernatant fluid is clear and light, the blood corpuscles have sunk to the bottom, and are not dissolved. The control must show definite solution of the blood. After a few hours slight solution of the agglutinated blood cor-

puscles may take place, even when the reaction is positive. If the tubes be not shaken the difference as compared with the control is very distinct, even at this stage. It is better, however, to read the result half to one hour after the occurrence of solution in the control test tube. In many cases, especially in syphilis undergoing treatment, the first effect is inhibition of solution; while there may or may not be a sedimentation. This is soon followed by solution. The presence of this feebly positive reaction enables no definite conclusion to be drawn.

A novice is advised to practice the reaction first of all on a case which is undoubtedly positive (preferably the blood of a paralytic) and one that is undoubtedly negative.

With regard to the utility of the Wassermann test as modified by Dungern, it has been placed in doubt by Münz as well as by Frühwald and Weiler, but has been recognised by Schultz-Zehden, Kepinow, Spiegel, Lampert and Steinitz. The communications of the last named authors show that the scale is turning definitely in favour of the utility of this modification. Still, further investigation is required to enable a definite solution of this question to be obtained. It is not just to recognise or to doubt the method by reason of a few experimental results, or from theoretical considerations. It deserves special attention from the fact that Steinitz describes it to be equal in reliability to Wassermann's method, while it requires no special practice on the part of the medical man who is using it.

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### **Sodii cacodylas.**

As an addendum to the account on page 15 of these Reports, reference will be made to a case of syphilis de-

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Münz, Deutsche medizinische Wochenschrift 1910, No. 37.

Frühwald - Weiler, Berliner klinische Wochenschrift 1910, No. 44.

Schultz-Zehden, Medizinische Klinik 1910, No. 27.

Kepinow, Münchener medizinische Wochenschrift 1910, No. 41.

Spiegel, Münchener medizinische Wochenschrift 1910, No. 45.

P. Lampert, Communication from the German hospital in Buenos Ayres.

Steinitz, Münchener medizinische Wochenschrift 1910, No. 47.

scribed by A. J. Caffrey in which sodium cacodylate proved of excellent service. The case was that of a young man with an ulcerating syphilide on the lower lip. The author's treatment consisted solely in subcutaneous injections of sodium cacodylate, no other local or internal treatment being employed. For 4 weeks or so the patient was given daily 0.06—0.12 gramme (1—2 grains) of the remedy, with the exception of 7 days on which the dose was increased to 0.18 gramme (3 grains). After the first injection the pain subsided and the ulcer began to heal, and after 4 weeks the patient was completely cured.

Special interest attaches to cacodylic acid treatment from a communication by Spencer L. Dawes and Holmes C. Jackson, which shows that Fraser's unfavourable criticism of cacodylic acid treatment is entirely unjustified, for it is based upon a few clinical trials, but not on careful physiological observation. It was shown, moreover, that sodium cacodylate might be given subcutaneously in comparatively large doses for a long time without harm. In a girl of 22 suffering from lichen ruber an injection was given every day for 6 days of 0.15 gramme ( $2\frac{1}{3}$  grains). This was followed for an equal period by double doses, then 0.45 gramme (7 grains) and finally 0.6 grammes (9 grains). This treatment was continued for 34 days, after which the dose was reduced to 0.3 gramme (5 grains) and four weeks later to 0.15 gramme ( $2\frac{1}{3}$  grains). Finally the patient was given only 0.05 gramme ( $\frac{3}{4}$  grain) every other day with additional intermissions. During 164 days a total of 42 grammes (630 grains) of sodium cacodylate had been injected subcutaneously. During this time the patient had gained 25 lb. in weight. She was discharged cured, and no relapse occurred. In psoriasis, eczema, chorea, malarial gastralgia, neurosis, anæmia, and even in pernicious and splenic anæmia the authors obtained good results as a rule with doses of 0.05 to 0.3 gramme ( $\frac{3}{4}$ —5 grain). In anæmia there was always an increase in the hæmoglobin in the blood.

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Caffrey, *Journal of the American Medical Association* 1910, 24th December, p. 2211.

Dawes-Jackson, *Journal of the American Medical Association* 1907, No. 25, p. 2090.

Fraser, see p. 5 of these Reports.



**Sodii choleinas.**

The cholagogue action of bile, or of sodium choleinate, when taken by mouth, is well known\*). So far, however, no trials have been made with its rectal application, and therefore the communications of K. Glässner and G. Singer are specially interesting. They found in experiments on animals that the rectal administration of bile had a marked effect on intestinal peristalsis, and they were led to try it on man. They state that the seat of the action of bile is the large intestine. The action of bile, however, depends, according to their investigation, on the biliary acids it contains, and consequently for therapeutic purposes the use of purified bile, i. e., sodium choleinate is to be recommended. The most convenient form for the practical use of bile salts was found to be suppositories containing 0.2 to 0.5 gramme ( $3\text{--}7\frac{1}{2}$  grains) of sodium choleinate.

The action of this drug is very characteristic. The authors chose for trial the most severe forms of habitual constipation and intestinal paresis in chronic bedridden patients. After 5 to 10 minutes, straining to evacuate the bowels sets in, and a motion is obtained the character of which indicates that the result of the rectal administration of bile acids very closely resembles the physiological action of defæcation. The authors never observed secondary effects on the general condition with the doses given above. In sensitive patients there was occasionally fairly severe tenesmus. The rapidity of the action and the large bulk of the fæces is often so considerable that in the case of patients who had been constipated for several days troublesome symptoms such as burning at the anus sometimes occurred and were clearly of mechanical origin. These slight inconveniences, however, would not occur on the methodical use of the drug. For sensitive patients the authors suggest the addition to the suppositories of a sedative, such as extract of hyoscyamus or belladonna, anæsthesin, etc.

Internally bile salts are said to have a less certain and regular action. The superiority of the rectal action is explained by the fact that the chief quantity of the sodium

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\*) See Merck's Index 1910, p. 188 and Merck's Reports 1906 and 1908.

Glässner-Singer, Wiener klinische Wochenschrift 1910, No. 1, p. 5. — Nouveaux remèdes 1910, p. 363.

choleinate taken internally is absorbed in the small intestine, while only small quantities reach the chief point of attack, the large intestine. Hence for administration by mouth a form should be selected which obviates this difficulty, and this may possibly be achieved by means of the use of hardened gelatin capsules.

### **Sodii chondroitin sulphas.**

Sodium chondroitin sulphate  $C_{18}H_{25}NSO_{17}Na_2$ , is a yellowish-white powder very readily soluble in water. It is not soluble in alcohol, ether and benzol\*). This salt is considered by Pons a very suitable test for albumin. Although there is no need for a new test for albumin, and sodium chondroitin sulphate is a substance the chemical characters and properties of which require more thorough investigation before it can be conscientiously recommended as a reagent, still Pons' method may be briefly described for the sake of completeness. If about 10 c.c. of the filtered urine to be tested are taken, and a drop of a 0.1 p.c. solution of sodium chondroitin sulphate and a few drops of acetic acid are added, in the presence of albumin an opacity occurs which slowly increases. The addition of acetic acid has the object of acidifying the mixture. If the urine gives a turbidity with dilute acetic acid alone, Pons directs that acetic acid be first added to it, and that it be then filtered before carrying out the test. A preliminary experiment with a suitable solution of sodium chondroitin sulphate is also to be recommended before applying the test.

### **Sodii glycocholas.**

The syphilis test known as the Porges reaction has awakened some interest of late, and will therefore be briefly described. The reaction, as given in the papers of H. Elias, E. Neubauer, O. Porges and H. Salomon, is carried out as follows:

The serum to be tested is cleared by centrifugalising, and is inactivated for half an hour at  $56^{\circ}C$ . An equal quantity

\*) See the article "Antituman" in these Reports, and Vierteljahresschrift für praktische Pharmazie 1910, p. 201.

Pons, Revue pharmaceutique des Flandres 1910, p. 73.

Elias, Neubauer, Porges, Salomon, Wiener klinische Wochenschrift 1908, p. 831.

of freshly prepared aqueous 1 p. c. solution of sodium glycocholate (Merck) is then added. If narrow precipitation tubes of 6 to 7 mm. diameter are used, 0.2 c. c. each of serum and glycocholate solution will suffice. This mixture must not be shaken; it is left for 16 to 20 hours at the temperature of the room. In a serum giving a positive reaction, distinct flakes will have formed by this time, and as a rule they form a mass at the surface of the fluid. Turbidity or traces of flaking are said by the author to be no evidence of a positive reaction, and definite microscopically visible flakes must be present. It is inadmissible to arrange the reagent and serum in layers, to use a warm incubator, to use reagents that are not freshly prepared, or to add phenol to them, while non-homogeneous turbid serum, and serum containing a very large amount of hæmoglobin should not be used.

F. Rosenfeld considers the Porges test a justifiable addition to the Wassermann test for the diagnosis of syphilis. It is distinguished from the Wassermann test by its relatively great simplicity, while it is not appreciably inferior to the Wassermann test in reliability. In any case the method should be more generally used. Tannhauser obtained satisfactory results with it. He regards the serum diagnosis as a very useful test, though in judging each individual case he insists on a knowledge of the clinical features before adopting specific treatment. The Porges test is described as worthy of note in the publications of Raimund and Schwarzwald, le Sourd and Pagniez and L. Merian. Raimund and Schwarzwald suggest that the Porges test be first used because of its simplicity, and if the result be doubtful to apply the Wassermann test.

### **Sodii iodas.**

The action of sodium iodate has been tested by A. Schiele for a number of years in various diseases of

Rosenfeld, Tannhauser, *Deutsche medizinische Wochenschrift* 1910, p. 164.

Raimund, Schwarzwald, *Wiener klinische Wochenschrift* 1909, p. 993.

Sourd, Pagniez, *Semaine médicale* 1909, p. 348.

Merian, *Medizinische Klinik* 1910, p. 1057.

Schiele, *Wochenschrift für Therapie und Hygiene des Auges* 1910, Vol. 13, No. 28 and 29.



the eye. He used a solution of 1:1000 with the addition of acoin by sub-conjunctival injection, which was repeated if necessary several times a day. In traumatic cataract this treatment was very successful. In incipient senile cataract the author tried it with some success. He obtained some improvement, but was unable to continue the treatment to the end for want of sufficient endurance on the part of the patients. In one case he was able to convince himself that the remedy did have the effect of clearing the lens. The solution is injected under the conjunctiva of the bulb in doses of 1 c.c., and is repeated every day or every second or third day according to the severity of the reaction.

### **Sodii perboras.**

A communication in Merck's Report\*) states that sodium perborate is an excellent agent for bleaching panama hats, and also straw hats. The method is as follows: The hats are first brushed with a solution of soap to remove the dirt. They are then thoroughly washed with clean water, and are dipped into a lukewarm solution of sodium perborate (3:450), and are left in this bleaching solution for 24 hours. Of course great care must be taken that the straw is completely covered by the fluid for parts which are not immersed assume a brown colour which cannot subsequently be removed. It is advisable to stir the bleaching bath from time to time. Before taking out the hat the solution is warmed up once more to about 50° C., when the hat is placed for a minute in an aqueous solution of oxalic acid (3:450). It is then washed with a large quantity of water, and dried in the sun. This method must be carried out in wooden or enamelled vessels.

### **Sodii peroxidum.**

A modification of the well known guaiacum resin blood test is described by B. Bardach and S. Silberstein. They first proved that the guaiacum test could be made considerably more sensitive by the addition of alcohol. They next sought to remedy the want of uniformity of the reaction

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\*) Merck's Report (New York) 1910, No. 5, p. 142.

Bardach-Silberstein, Zeitschrift für physiologische Chemie 1910, Vol. 65, p. 511.

due to the varying character of oil of turpentine by using a suitable substitute for oil of turpentine so as to render the action more reliable. The best substance for this purpose was found to be sodium peroxide. The test is carried out as follows:

To about 5 c.c. of the fluid to be examined are added a few drops of a freshly prepared alcoholic solution of guaiacum resin until the fluid on mixing begins to look opaque. A pinch of sodium peroxide is then added by means of a glass spoon. Acetic acid (30 p.c.) is then quickly added in sufficient quantity (about 2 c.c.) to produce an acid reaction, and 1 to 2 c.c. of alcohol are carefully layered on to the surface of this mixture. Even when very small quantities of blood are present a blue ring appears at once at the juncture of the two fluids. This blue colour appears after 1 to 2 minutes at the latest, and usually changes to green or to a dirty colour. The authors insist that the acetic acid and alcohol should be added rapidly while there is still a strong evolution of gas. The limit of the sensitiveness of the guaiacum turpentine reaction is reached with a proportion of 30 milligrammes of blood to a litre of water, and with the test now described the presence of 7 milligrammes of blood is said to be demonstrable in a litre of water. It is well to test the sodium peroxide to be used for this purpose by itself, i. e., without blood. In doing so no more than a slight green colour should be produced.

### Sophol.

O. v. Herff has repeatedly advocated the treatment of ophthalmia neonatorum with sophol, for he has obtained very satisfactory results with this remedy in a large number of cases. His method is very simple. One or more drops of the 5 or 10 p.c. solution are placed on the closed eyelids, or in the inner angle of the eye. The eye is then opened by slight traction if the child does not open its eye spontaneously. It is necessary for the edges of the lids and the eyelashes to be thoroughly flooded with the solution, for it is here that the gonococci settle at first. Sophol is of importance not only as a curative agent, and the author has

used it with success in about 100 cases of conjunctivitis caused by various bacteria.

Other communications on the sophol treatment of gonorrhœal ophthalmia have been published by J. F. Moran, S. v. Gratkowski and Grünbaum. They all confirm the advantages of sophol as described by Herff\*).

### Spirosal.

The treatment of rheumatic diseases by spirosal has been studied by W. Klein, J. Daniel, Walter and Raschkow. Walter found spirosal, when applied endermatically, to differ from mesotan, which causes severe inflammation of the skin in sensitive persons, by being entirely non-irritant, no matter whether it is applied by rubbing or by painting. It has the further advantage of being free from odour. In muscular rheumatism and chronic articular rheumatism the author found it to have a prompt sedative action. In afebrile, acute and sub-acute cases with little swelling of the joints, it led to the subsidence of the trouble very quickly. Walter always used an alcoholic solution of spirosal 1 + 2, as issued ready for use. Klein tried spirosal in the most varied rheumatic affections, both slight and severe, and was successful in every case. In severe cases of articular rheumatism the effect was not so definite, still there was an undoubted improvement in every instance. The author's statistics contain one remarkable case of "gonorrhœal rheumatism" in which a rapid cure was obtained by spirosal treatment. Daniel, who also prescribed spirosal with success in rheumatism, applied the remedy by rubbing twice a day in rheumatic affections, using a woollen cloth; in neuralgia he painted it upon the part. In a tabetic patient with severe lightning pains, spirosal also gave excellent results. Finally the therapeutic value of spirosal in rheumatism is fully confirmed in the communications of Raschkow.

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Moran, Virginia Medical Semi-Monthly 1910, 22<sup>nd</sup> April.

Gratkowski, Dissertation Breslau 1910.

Grünbaum, Münchener medizinische Wochenschrift 1910, No. 15.

\*) See Merck's Reports 1906—1909.

Klein, Deutsche medizinische Wochenschrift 1910, No. 48.

Daniel, Allgemeine medizinische Zentral-Zeitung 1910, No. 12.

Walter, Die Heilkunde 1910, No. 2.

Raschkow, Berliner klinische Wochenschrift 1910, No. 52.



Såg prescribed spirosal in ear practice for many cases of furunculosis of the external auditory meatus. For this purpose he placed a small strip of gauze in the meatus, and dropped upon it 2 to 3 drops of the alcoholic solution of spirosal 4 to 5 times a day. In this way a fresh solution was continually brought into contact with the affected auditory meatus, and was able to display its disinfectant action. In commencing folliculitis the preparation also yielded good results, but in this case a combination of spirosal with coryfin is more active in disinfectant power, and is consequently to be recommended.

### **Strophanthin.**

In a paper on the practical use of strophanthin in therapeutics, Kotschalowski showed that injections of the glucoside in therapeutical doses are harmless, and are not more painful than injections of any other preparation which causes no pain in itself. The action of strophanthin injections on the heart was always apparent within a remarkably short time, with the exception of one case of paroxysmal tachycardia. This was the case even when digitalis substance had been given previously without effect. The action showed itself in greater freedom of respiration, and in the subsidence of the palpitation. Further, the frequency of the pulse was reduced and its amplitude increased; the blood pressure did not rise to any extent. Diuresis was increased, however, and with it there was a diminution or complete disappearance of the cyanosis. The duration of the action of strophanthin injections was at least 3 hours, and in extreme cases it continued for 8 days. In the author's opinion strophanthin is a remedy with an energetic action; it should be given, not in every case of heart disease, but only in cases in which an immediate, rapid action is found necessary, e. g., in conditions of acute asystolia in uræmia and in infective diseases. (Further details on the use and dosage are given in Merck's Reports 1904—1909, or Merck's Index, 1910, p. 242.)

Experiments on the action of medicinal doses of strophanthin on artificially lowered blood pressure have been carried

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Såg, Budapesti Orvosi Ujsag 1910, No. 7.

\*) See the article "Coryfin" p. 150.

Kotschalowski, Medizinskoe Oboshrenie 1909, No. 6

out by H. Straub. His results are best studied in the original paper, as they cannot be reproduced in a short abstract.

Danielopolu also gives practical details regarding the use of strophanthin in heart disease. His communication contains nothing new. In general he confirms the value of injections in cases which call for rapid aid. He considers that the remedy should be avoided when the patient is under the action of digitalis, for in such cases toxic symptoms are readily produced. His highest dose of 1 milligramme ( $\frac{1}{64}$  grain) in 24 hours is in agreement with that given by most other authors. His statement that amorphous strophanthin is considerably less poisonous than the crystalline preparation would be very difficult for the author to prove (see Merck's Reports 1909, page 321—324).

### Strychnine.

Strychnine and its salts have been applied therapeutically in various gastric and intestinal affections. B. Polák carried out a pharmacological investigation to ascertain definitely the action of the alkaloid on peristalsis. This question has already been attacked by various workers, but their results are contradictory in certain respects. The present author's experiments on frogs and rabbits confirm the view expressed some time ago by Nasse. In 24 experiments doses of 0.0005 to 0.01 gramme of strychnine nitrate were injected subcutaneously into frogs, while at the same time the same amount was given to 23 other frogs by mouth. It was found that small doses had no effect on the movements of the stomach and intestines; even large doses produced no peristaltic movements in the intestines. Experiments on isolated frogs' stomachs also gave negative results, as did experiments on rabbits. In the latter, even after large doses, peristalsis became weaker and weaker, and in some cases left off entirely. Even during general tetanic strychnine convulsions, the intestines remained absolutely at rest. These results show that the use of strychnine for the purpose of exciting peristalsis had no foundation. Consequently the only reason re-

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Straub, *Therapeutische Monatshefte* 1910, No. 3.

Danielopolu, *Revista scintelor medicale* 1910, February.

Polák, *Klinisch-therapeutische Wochenschrift* 1910, No. 49.

maintaining for giving it is its use as a bitter remedy, but for this purpose it has no advantage over other bitters in gastric and intestinal diseases.

In neuritis G. H. R. Dabbs has obtained good results with injections of strychnine. He injects 0.0005 to 0.0006 gramme ( $\frac{1}{120}$ — $\frac{1}{100}$  grain) of strychnine nitrate twice a day in aqueous solution along the affected nerve. This treatment is said to give a successful result within four weeks at the longest.

In pneumonia in old people W. F. Waugh looks for particularly good results from strychnine because of its stimulant properties and its action in increasing the effects of antipyretics. For this purpose he uses strychnine arseniate. According to the condition of the individual case, he prescribes 0.0005 gramme ( $\frac{1}{120}$  grain) of this remedy every 15, 30 or 60 minutes, until the successful result appears. Occasionally the tonic action is said to show itself after three doses, but sometimes a total quantity of 0.06 gramme (1 grain) of strychnine arseniate has to be taken before the action is apparent.

### Stypticin.

In uterine hæmorrhage stypticin is a favourite remedy among the drugs used at the present time; especially when the cause of the hæmorrhage is known the preparation may be used with satisfactory results. If the result is unsatisfactory, it is necessary to ascertain before proceeding whether the remedy has not been used without sufficient thought, and whether ergot would not have given better results. R. Asch found stypticin especially suitable in venous hæmorrhage, no matter whether the hæmorrhage persists too long or recurs too frequently. The author states that stypticin, a derivative of narcotine, has no power of exciting contraction, either on the smooth muscles of the uterus or on the vessels. It is this property of relaxing the muscles that makes it useful in cases of venous congestion for checking hæmorrhage where ergot would cause muscular contraction which would compress the veins without compressing the arteries to

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Dabbs, British Medical Journal 1910, No. 2516, p. 260.

Waugh, Semaine médicale 1910, p. 283. — Clinica castellana 1910, p. 165.

Asch, Der Frauenarzt 1910, No. 8, p. 338.



the same extent. Hence it is indicated in arteriosclerosis and in certain cases of chronic metritis. In this case it will set free the compressed veins by relaxing the muscles; thus it will favour the return of blood, and so act as a hæmostatic. Asch's experience shows the remedy to possess an excellent action in general diseases for the relief of venous congestion in the whole organism, in heart disease, emphysema and diseases of the liver. This is especially the case in heart disease if the remedy be prescribed prophylactically at the proper time before menstruation is expected, for in the days preceding menstruation it acts to special advantage by postponing the appearance of the hæmorrhage for several days. Five tablets, (each containing 0.05 gramme [ $\frac{3}{4}$  grain]) are given daily for 4 to 5 days before the onset of menstruation; this quantity is enough to cause the hæmorrhage to commence 2 to 4 days later. Stypticin is then given again before the next menstrual period, and this is repeated until menstruation has returned to the normal periods. In heart disease, if menstruation is excessive, the use of the preparation may be continued by mouth, or if necessary, subcutaneously or intramuscularly. In hæmorrhage due to increased venous congestion caused by retroflexion which cannot be put right for one reason or another, the remedy is effective, provided the change of position has not existed long enough to produce swelling of the mucous membrane, or to lead to displacement of the vessels as the result of disease of the appendages or of parametritis. Very satisfactory results with stypticin in uterine hæmorrhage are described by H. J. Berger and Robert.

### Substitol.

In an interesting paper on the significance of the inflammatory effects of early carcinoma, S. Bergel points out that infective inflammation such as affects carcinomatous or sarcomatous tissues, may frequently give rise to a diminution or even complete disappearance of the tumour. It is probably permissible to assume that in a particular stage at any rate

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Berger, Therapeutic Gazette 1909, 15th August.

Robert, Gazette des hôpitaux 1910, No. 21 and 26.

Bergel, Medizinische Klinik 1910, No. 6, p. 221.

inflammation is the natural attempt of the organism to get rid of the tumour, just as in the case of a foreign body. This view is all the more probable since cancerous tumours, so long as they are surrounded by a layer of inflamed tissue, are not able to produce dissemination of cancer cells, or to form metastatic growths. The idea hence suggests itself, in cases in which cancerous tumours are only partially surrounded by inflammatory tissue, to excite aseptic inflammation, with the object of setting up a curative effect in the treatment of carcinoma, although the effect may be insufficient. A convenient, harmless and natural remedy for achieving a measurable aseptic inflammation, with great leucocytosis, serous or fibrinous exudation, fibroblasts and newly formed connective tissue, has been found by Bergel in the injection of fibrin. It is well known that attempts have been made earlier, with some success, to affect malignant tumours by injections of blood, but the serum and the red blood corpuscles when injected frequently gave rise to toxic symptoms. Neither are they able, like fibrin, to give rise to the typical symptoms of acute aseptic inflammation with leucocytosis and newly formed connective tissue. The poisonous action is completely prevented by using fibrin. Repeated injections of the same sort of fibrin do not lead to anaphylaxis, or to other injurious effects on the organism. Fibrin is the only constituent of blood which has the power of producing this purely aseptic inflammation. The use of fibrin in the form of a powder such as substitol is harmless, rational and effective for the preparation may be obtained in a sterile, stable form ready for use, and in a concentrated form so that very much smaller quantities give far greater doses of the active substances. Thus 1 litre of horse's blood contains about 4 grammes (60 grains) of dry fibrin; the injection of a dose of 0.3 gramme (5 grains) of substitol in emulsion would correspond to the amount of fibrin contained in 75 grammes ( $2\frac{1}{2}$  oz) of blood.

Experiments on dogs showed that substitol injections led to a well marked inflammation with regressive changes in the nodules. The examination of these nodules showed mortification of a very large part of them, disintegration in their neighbourhood, and the presence of a limited inflammation, while certain parts of the tumour still showed carcinomatous tissue.

After these experiments Bergel used substitol in man. To enable him to gauge the action of the preparation correctly in inoperable, recurrent mammary carcinoma, he used fibrin injections in a part of the tumour while he left another part untreated. The latter continued to grow, while the parts treated showed not only inhibition of growth, but also a definite shrinking and destruction of the carcinomatous tissues, which were cast off, while the base of the tumour was limited by inflammation and by epithelial formation. If a cancerous nodule about the size of a hazel-nut be treated under the technical conditions previously\*) described by the author, and about 0.4 to 0.5 gramme (6 to 7½ grains) of substitol suspended in 8 to 10 grammes (140 to 170 min.) of normal saline solution injected, the author states that the following appearances may be observed: "There is moderate pain for a short time with slight rise of temperature, coming on as a rule after 6 to 12 hours, and lasting no longer than one to two days. An œdematous swelling then occurs at the seat of the injection, and around it, but there is no severe inflammatory redness. As a rule the carcinomatous nodule cannot be distinguished from its somewhat dough-like surroundings; it is practically impossible to feel it. This condition persists for several days, and even after the œdema has begun to pass off, after 4 to 5 days, it is as a rule still impossible to feel the borders of the tumour. After the swelling has completely subsided the carcinomatous tissue is felt to be smaller, shrunken and occasionally somewhat fluctuating."

Another significant fact is that Bergel never found the nodules he had treated to increase in growth subsequently. He was able to show that the nodules continue to grow more slowly than those that had not been treated. The microscopical investigation of tumours treated with substitol showed the undoubted good effect of the treatment. For this reason Bergel regards a further trial of the fibrin treatment of carcinoma to be desirable and justified.

Wagner reports on a contusion of the right hand by

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\*) See Deutsche medizinische Wochenschrift 1909, No. 31, p. 1349.

— Merck's Reports 1909, p. 97.

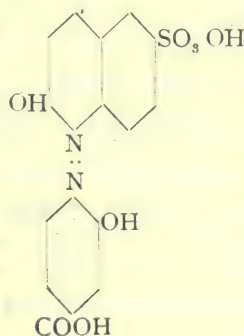
Wagner, Medizinische Klinik 1910, No. 10, p. 390.



a threshing machine, which was first treated with hydrogen peroxide, corrosive sublimate baths, etc., but showed poor granulation. He feared necrosis of the exposed tendons and of the bones which were bared of their periosteum. He therefore covered the wound every day with a thin layer of substitol after syringing it with hydrogen peroxide. After the second application granulation commenced which covered the bare tendons and bones in about 14 days. The total result of the substitol treatment was satisfactory.

### 6-Sulpho- $\beta$ -naphtholazo-m-oxybenzoic acid.

This acid has been shown, by the experiments of R. Mellet, to be of use as an indicator in alkalimetry and acidimetry, for in dilute aqueous solution it gives with alkalies a deep violet colour, and with acids an orange-red colour. The chemical composition of the acid is apparent from its formula:



As an indicator a 1 p. c. solution of the sodium salt is used, to which is added enough  $\frac{1}{10}$  normal hydrochloric acid to impart a definite red colour. As compared with litmus, the colour of this solution is said to be 30 times more intense. Moreover the author points out the following fact as resulting from his tests: The new indicator is quite sensitive enough for use with  $\frac{1}{100}$  normal solutions. The quantities of normal solutions used correspond with the quantities required with phenolphthalein if the change of colour be carried through to the extreme colour. Hence these two indicators can replace one another. Whatever dilution is present, the indicator always shows practically

the same sensitiveness up to a total volume of fluid of about 80 c. c. The titration may be performed with equal exactitude in both directions, provided the titration be carried through to the extreme change of colour. The change from extreme red to extreme violet, and inversely requires less normal solution than in the case of other indicators, that is to say the transition colours lie between narrower limits. In this respect there is no material advantage over phenolphthalein, and practice must show whether the new indicator fills a real need.

### Sulphoform.

Triphenylstibine sulphide  $(C_6H_5)_3SbS$ , issued under this name, is an organic compound of sulphur and antimony, consisting of white crystals. It was first prepared by L. Kaufmann. The preparation is fairly stable, but it possesses the property of liberating sulphur as the result of very slight chemical influences, even when it merely separates out from its solutions (in oil or alcohol), and triphenylstibine  $(C_6H_5)_3Sb$  is formed. Kaufmann had the idea of using the preparation for dermatological purposes, as a specially intense action might be anticipated from sulphur in the nascent state. His physiological and chemical investigations justify this assumption, for he found that triphenylstibine sulphide had the property of setting oxygen free from hydrogen peroxide with extreme ease, sulphur separating out and becoming oxidised to sulphuric acid, while the antimony residue was oxidised at the same time to oxide of antimony which combined with the sulphuric acid. This reaction takes place quantitatively at a temperature of 36 to 37° C. Compared with the power of ordinary sulphur of withdrawing oxygen, triphenylstibine sulphide is more than 100 times as efficacious.

Sulphur takes the first place among all remedies recommended for the treatment of seborrhœic alopecia, no other remedy being comparable with it in efficacy. M. Joseph consequently recommended triphenylstibine sul-

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Kaufmann, Berichte der deutschen chemischen Gesellschaft Berlin 1908, Vol. 41, p. 2762. — Biochemische Zeitschrift 1910, Vol. 28, p. 67.

Joseph, Dermatologisches Zentralblatt 1910, Vol. 14, No. 1, p. 2 and No. 2, p. 34.

phide most strongly for this purpose. His method is as follows: When the hair is quite dry, pure castor oil or olive oil is applied to it by means of a pledget of wool, while in case of greasy hair a mixture of equal parts of castor oil and absolute alcohol is used. After this preliminary treatment the skin of the head is cleansed of scales the first evening by means of spirit of soap and warm water. The soap is removed with water, and a quarter of the skin of the scalp is prepared with castor oil. An ointment is then applied consisting of 1 gramme (15 grains) of sulphoform, 2 drops of oil of rose and 9 grammes (135 grains) of American white vaseline. The other three-quarters of the head are treated on the following three days. On the fifth day the first quarter of the head is taken in hand once more. In the morning the grease is washed away with neutral soap, and a solution of 1 gramme (15 grains) of resorcin in 50 grammes ( $1\frac{2}{3}$  oz) of spirit of lavender and 50 grammes ( $1\frac{2}{3}$  oz) of spirit of rosemary is applied. With this treatment the formation of crusts and the falling out of the hair is said to diminish considerably after a very short time. For subsequent treatment the author recommends the use every morning of a hair wash (4 grammes [70 min.] of tinctura cantharidis, 50 grammes [ $1\frac{2}{3}$  oz] of spiritus lavandulæ and 50 grammes [ $1\frac{2}{3}$  oz] of spiritus rosmarini), and every evening the application of oil of sulphoform (1:10).

Applied as a 5 to 20 p.c. ointment, sulphoform is useful in various forms of eczema, impetigo simplex, and pityriasis rosea. In impetigo contagiosa a mixture of 20 parts of sulphoform and 80 parts of zinc oxide paste is used.

### **Taka-diastase.**

The therapeutic value of taka-diastase in intestinal fermentative dyspepsia is described by A. Alexander from his own experiences\*). He found the prolonged administration of the remedy of great value in starch dyspepsia, a condition readily recognised by the presence of undigested starch residues in the stools. After 8 to 10 days the stinking, thin fluid stools containing starch were put right. After about four weeks no starch and no mucus were found

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Alexander, Therapie der Gegenwart 1910, No. 12, p. 537.

\*) See Merck's Index 1910, p. 94.



in the stools even after the discontinuance of the diastase treatment. In two cases in which a tendency to diarrhoea returned the author obtained the final subsidence of the diarrhoea by renewing the use of the taka-diastase. In the presence of achylia the administration of hydrochloric acid did not give the desired result until taka-diastase was given simultaneously. In a case of hyperchlorhydria with catarrh of the small intestine in which the stools contained a large quantity of starch, the author found that the administration of taka-diastase with pankreon led to a rise in weight of 15 lbs. in seven weeks, while the diarrhoea left off altogether.

Taka-diastase is best given after meals in doses of 0.2 to 0.3 gramme (3—5 grains) (see Merck's Reports 1896, page 145, and 1897, page 140).

### **Tanargentan.**

In a ten-year-old horse with chronic diarrhoea that had been treated without benefit by diet, care, and various drugs, including opium and silver nitrate, K. Schade gave as a last resource tanargentan\*) with entire success. He prescribed it on three consecutive days in doses of 10 grammes ( $\frac{1}{3}$  oz) daily. On the third day of treatment a marked improvement set in. He then made a pause of three days and followed this by giving 7 grammes (105 grains) more on each of the next two days. On the following days the appetite and evacuations became normal, and the animal made a rapid recovery.

### **Tannyl.**

An exhaustive pharmacological investigation of this preparation\*\*) has been carried out by R. Veit. His results are given in the following conclusions: Tannyl is little affected by the gastric juice. In the alkaline intestinal juice, however, it is gradually split up into its components. In this way the lower parts of the intestines are brought under the active influence of the products of its decomposition. Even in large doses the remedy causes no unpleasant secondary

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Schade, Deutsche tierärztliche Wochenschrift 1910, No. 44, p. 655.

\*) See Merck's Reports 1909.

\*\*) See Merck's Reports 1908 and 1909.

Veit, Dissertation Giessen 1910.

effects. In dogs it has given excellent results as an astringent and antiseptic in the treatment of various gastro-intestinal diseases. Even the obstinate diarrhoea of distemper was put right quickly and certainly by its aid.

### **Thallii carbonas.**

A sensitive reagent for carbon bisulphide has been suggested by E. Kurowski. It is prepared by boiling thallium carbonate ( $\text{Ti}_2\text{CO}_3$ ) with a solution of acetyl-acetone ( $\text{CH}_3\cdot\text{CO}\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$ ) in alcohol for some time. An alcoholic solution of acetyl-acetone thallium ( $\text{CH}_3\cdot\text{CO}\cdot\text{CTi}_2\cdot\text{CO}\cdot\text{CH}_3$ ) is thus obtained. This solution gives with carbon bisulphide a voluminous orange-yellow precipitate. With traces of carbon bisulphide in any fluid, a mere yellow turbidity or colour is obtained. By this test a single drop of carbon bisulphide in a litre of benzol may be detected. It is true the reagent gives precipitates with other organic compounds of sulphur, but the author states that their colour is different from that produced by carbon bisulphide.

### **Thilaven.**

A few years ago a new preparation of sulphur was described by F. Nagelschmidt under the name of "Thiozon". It is said to be distinguished by the large amount of absorbable sulphur it contains. Its chemical constitution was accurately described by him, and explained theoretically. This preparation is now on the market under the name of "Thilaven", and has been recommended for gynæcological purposes by R. Knorr. He states that it contains about 5 p.c. of sulphur, and has an agreeable odour.

Thilaven is said to be of use, added to the water of the bath, or in the form of a glycerin solution, in various diseases of women, such as chronic sub-acute inflammation in the pelvis, parametritis retrahens, parametritis exsudativa, perimetritis, oöphoritis, salpingitis, metritis, adhesions, etc. Knorr found its action as good as that of other preparations of sulphur previously used therapeutically. To prepare a large bath the author poured 50 to 60 c.c. of thilaven into the bath after the patient's skin had become somewhat

Kurowski, *Chemik Polski* 1910, p. 193.

Nagelschmidt, *Therapeutische Monatshefte* 1908, p. 520.

Knorr, *Medizinische Klinik* 1910, p. 669.

sodden by the warm water. For sitzbaths he prescribed 20 c.c. The 5 p.c. or 10 p.c. thilaven-glycerin was used by him in suitable cases for plugging the vagina. This process and the baths are said to agree well in all cases.

### **Thiocyanates.**

Regarding the dosage of the thiocyanates, and their toxicity, we have, as yet, no absolutely trustworthy data. Of late more interest seems to be taken in sodium thiocyanate\*), hence a careful pharmacological investigation of this salt is particularly desirable. The uncertainty regarding the toxicity or otherwise of the thiocyanates is apparent from the literature, and certainly acts as a deterrent to their use. During the past year I received several enquiries regarding this point, but for the reasons stated I was not able to furnish a satisfactory answer. Hence a communication by O. Adler is interesting, in which he shows that ammonium thiocyanate is not very poisonous. A man of 24 had taken a solution of 30 grammes (1 oz) of ammonium thiocyanate in 200 c.c. ( $6\frac{2}{3}$  oz) of water in a single dose. After a quarter of an hour vomiting set in and was repeated after 6 hours. With the exception of slight giddiness no symptoms of poisoning occurred, either at once or during the 14 days that followed, although thiocyanates were abundantly detected in the urine during the whole of this time. Although the main bulk of the salt was probably evacuated at the first attack of vomiting, the danger of the thiocyanates is still rendered very doubtful by this case. Neither is proof afforded by this case that they are non-poisonous.

Zoltan, Pauli and Pal have recommended sodium thiocyanate for the treatment of arterio-sclerosis; it lowers the blood pressure. The daily dose used is 0.5 to 3 grammes ( $7\frac{1}{2}$ —45 grains) (in 150 c.c. [5 oz] of water).

### **Tinctura pyrethri rosei.**

In health and summer resorts, and also in towns, no measure is left untried to deal with the increasing plague of gnats

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\*) See Merck's Reports 1909, p. 316.

Adler, Deutsche medizinische Wochenschrift 1910, No. 48, p. 2271.

Zoltan, Merck's Reports 1909, p. 289.

Pauli - Pal, Archivio per le malattie di cuore, dei vasi e del sangue (Bordighera) 1910, No. 1, p. 27.



either by destroying them or by rendering their bites as far as possible harmless. As a rule, the usual well known remedies are used, and are recommended anew. Thus B. Lewy has once more suggested *tinctura pyrethri rosei* as an effective remedy. It has possibly passed into oblivion to some extent. Formerly it was dropped into water and used for washing, to keep the troublesome insects off for a time. The author tried rubbing the tincture into the skin, and found that this manipulation afforded protection for 4 to 5 hours, and — an important consideration — caused neither poisoning, nor exerted an irritant action on the skin.

### **Tropacocainæ hydrochloridum.**

Further communications on lumbar anæsthesia with tropacocaine have been made during the past year by O. Heinz, E. Slajmer, B. R. v. Arlt, and J. T. Morrison. They all confirm the advantages of tropacocaine already explained in these Reports\*).

Slajmer gives a survey of the use of tropacocaine in spinal anæsthesia, its great value, the dosage, and method of applying it. His paper is of special interest because the author may be regarded as an authority on this subject. He reports on 2700 lumbar anæsthesias with the remedy. Of these 1278 were for radical cure of hernia, 157 for incarcerated hernia, 129 for amputations and resections, 167 for laparotomies, 171 for appendicitis operations, etc. As is well known, the method has been found useful in all operations on the lower half of the body. It is of special importance in elderly persons with diseases of the heart, kidneys and lungs, in whom a general anæsthetic might give rise to danger. Arterio-sclerosis and severe cases of diabetes mellitus form no contra-indication, but the author regards acute septic processes, severe fever of unknown cause, florid syphilis and tuberculosis as contra-indications. He always used sterile ampoules containing 0.05 and 0.1 gramme of

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Lewy, *Zeitschrift für Balneologie, Klimatologie und Kurorthygiene* 1910, p. 443.

Heinz, *Wiener medizinische Wochenschrift* 1910, No. 37.

Slajmer, *Beiträge zur klinischen Chirurgie* 1910, Vol. 67.

v. Arlt, *Münchener medizinische Wochenschrift* 1910, No. 28.

Morrison, *Lancet* 1910, 10<sup>th</sup> September.

\*) See Merck's Reports 1892—1909.

tropacocaine in normal saline solution. In by far the greater number of cases 0.07 gramme was the dose used, in a good number of cases 0.5 and 0.8 gramme, while smaller or larger doses were seldom used. With this dosage no fatal case occurred that could be even partially attributed to the anæsthetic. In 7 cases only the author observed severe collapse, and this occurred chiefly in patients in whom the operation was performed with the pelvis raised to some extent. Difficulty in evacuating the bladder did not occur more frequently than in the case of other narcotics. Slight headache occurred in 25 p. c., prolonged headache in 2 p. c. of the cases. Like other authors, Slajmer lays special importance on the method of carrying out spinal anæsthesia. If the puncture be made accurately under strictly aseptic conditions, and care be taken that no chemical or mechanical irritants reach the subdural space, and if a sufficient quantity of solution be injected, it is possible to reckon confidently on a satisfactory anæsthesia of sufficient duration (up to 2 hours). No special complications will occur, and there will be no failures. Where local anæsthesia is applicable, Slajmer recommends its use, as spinal anæsthesia is always a more serious matter. In choosing subjects for spinal anæsthesia v. Arlt considers the quality of the patients of great importance. This concerns especially age, strength, psychological condition and intelligence. With regard to the technical details he recommends a special set of instruments which permit of the greatest possible asepsis and exclude any evil consequences. To prevent the danger of toxic effects in children and feeble patients the author has hit on the following method:

“After injecting the tropacocaine solution I leave the needle *in situ* and test the degree of analgesia. As soon as it has attained the desired height (it advances toward the head) I allow as much, or rather more, than the quantity of fluid used for the injection to escape, with the object of removing the tropacocaine that has not yet been absorbed. Professor Pregel has been good enough to ascertain by exact weighing that the liquid obtained in 4 cases, corresponding to a quantity of injection fluid of four times 0.07, i. e., 0.28 gramme, contained 0.067 gramme of tropacocaine hydrochloride which could be crystallised out. This amounts to the withdrawal of 25 p. c. of the tropacocaine used. Hence the whole of the tropacocaine was brought into action, but only 75 p. c.

of it was absorbed and able to produce toxic symptoms. So far I am able to state that the intensity and the duration of the analgesia was not lessened by allowing the excess fluid to escape, and no severe cases of poisoning occurred, although I injected full doses in children of 7 to 10 years. A further account of this modification will be reported by me later, founded on a larger number of observations”.

Morrison prefers tropacocaine to all other anæsthetics, for it is the least poisonous. In 173 cases he encountered no case that assumed a threatening character, although he used spinal anæsthesia in patients of 10 to 80 years. G. A. Wagner also considers tropacocaine to have the advantage of being a safe substance for use in spinal anæsthesia, apnœa and collapse occurring very much less frequently following its adoption. For this reason Heinz also used tropacocaine. His results are fully in accord with those of the above named authors.

### Trypsin.

The trypsin treatment of tuberculous affections is described by Schiller, A. Brüning and Sohler. Schiller found tuberculous abscesses to differ from hot abscesses in being poor in ferment. Hence it is necessary to introduce a ferment to dissolve the albumin of the pus so as to make it capable of absorption. For this purpose trypsin is suitable. It should be injected into the abscesses in a 1 p.c. sterile solution. The abscesses are punctured, the pus withdrawn or aspirated, and freshly prepared trypsin solution with normal saline solution is injected. The pus must be removed every day, the injection of trypsin carried out every other day. In tuberculous abscesses of the soft parts 3 to 5 injections are required, as a rule, though the author occasionally found a single injection sufficient. The trypsin injections are said by Schiller to be painless, and they only cause fever at the beginning of their use. They are said to act better than iodoform injections, they quickly limit the secretion of pus, and they cause granulations to form. In

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Wagner, Monatsschrift für Geburtshilfe und Gynäkologie 1910, Vol. 33, No. 6.

Schiller, Klinisch-therapeutische Wochenschrift 1910, No. 10.

Brüning, Deutsche medizinische Wochenschrift 1910, No. 35.

Sohler, Münchener medizinische Wochenschrift 1910, No. 46.



tuberculous diseases of joints this method failed. Sohler came to the same conclusions. In his experience trypsin is in these cases unsuitable because its injection gives pain, while its solutions are unstable and consequently dangerous, and he saw toxic symptoms now and then. The softening of the tissue affects first the diseased, disorganised tissue beset with tuberculosis, but it does not stop short at the healthy tissues. Loosening of the joint cartilage is thus brought about which prejudices rather than advances the prospect of a cure. The prospect is also prejudiced by the pus penetrating into the soft parts. The secondary effects are obtained quite as well with less pain and with less danger by chemical means.

Brüning has been led by his experiences to the conclusion that trypsin injections give good results in the treatment of tuberculous hygromata and small cold abscesses. Even a focus of diseased bone may be made to heal if it is not too great. In depressed abscesses trypsin is not superior to iodoform-glycerin. Joint tuberculosis with large foci of disease in the bones, or pure fungi are found unsuitable for treatment with trypsin injection, neither is any good to be expected from this treatment in caseous or hard lymphomata.

Failures in the treatment of cancer by trypsin\*) are attributed by Beard to the small dosage of trypsin and amylopsin. He draws attention to the excellent results obtained by F. W. Lambelle with large doses, and he points out that this is a method which should be tried more thoroughly. It is obvious that various open questions regarding trypsin treatment still remain to be answered.

### Unna's Skin reagents.

To test the reaction and function of the skin, P. G. Unna and L. Golodetz have found the following tests of use:

Nile red is obtained by dissolving 0.25 gramme of

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\*) See Merck's Reports 1906—1909.

Beard, communication in a letter.

Lambelle, *Journal of the Royal Army Medical Corps* 1909, Vol. XIII, p. 71 and 1910, Vol. XIV, p. 316.

Unna-Golodetz, *Monatshefte für praktische Dermatologie* 1910, Vol. 50, No. 10, p. 451.

Nile blue sulphate in 10 grammes of alcohol 96 p. c., and adding one drop of half normal alcoholic solution of potassium hydroxide, then adding 30 grammes of liquid paraffin, and warming on a steam bath until the alcohol has evaporated. After cooling, 30 grammes of xylol are added. The reagent thus obtained has a red colour which turns to blue on contact with substances having an acid reaction. It is hence suited for detecting the acidity of the horny layer, and for the preparation of test papers for showing the acid reaction of the cutaneous secretion.

Chrysophan yellow is the name given by Unna to a solution of nitro-chrysophanic acid. It is obtained by dissolving 1 gramme of nitro-chrysophanic acid in 100 grammes of xylol, and adding 100 grammes of liquid paraffin. This yellow reagent serves for the estimation of the reducing power of the skin. Its colour turns to red, not only under the action of reducing substances, but also by that of alkaline bodies. It must therefore be acidified with acetic acid before use.

Rongalite white is the name given by Unna to a reagent used for determining the oxidising power of the skin. For its preparation 1 gramme of methylene blue is dissolved in water, 2 grammes of rongalite (the sodium salt of sulphonylic acid combined with formaldehyde) are added and the whole is heated to boiling. After a short time the mixture loses its colour, sulphur separating out. After filtering, the fluid thus obtained forms a slightly yellow solution with an acid reaction. It contains an excess of rongalite, and does not turn blue on exposure to air. Alkalies favour the oxidation of the reagent by the oxygen of the air. Hence it is necessary to add an acid to prevent mistakes. This solution of leuco-methylene blue becomes blue under the oxidising action of the cutaneous secretion, while at the same time skin laden with such secretion is similarly stained with the colour of methylene blue.

### Urotropine.

In administering urotropine, R. Hilbert observed the occurrence of a rash in the presence of an idiosyncrasy. He reports the case because this secondary action of the remedy

has not yet become known. He had given a pregnant woman a tablespoonful of a 5 p.c. solution of urotropine with the result that a rash appeared over the entire body with severe itching and burning pain, causing tears to flow, and headache. In a second attempt with the same drug the same appearances showed themselves and disappeared after 8 hours.

Like Crowe, S. Stockmayer considers urotropine treatment a useful measure in purulent meningitis, for use in conjunction with metallic ferments and streptococcic and meningococcic serum. J. Ibrahim agrees with this view. He used urotropine particularly in meningitis in children. His results agree with those of Crowe in that he was always able to detect urotropine in the cerebro-spinal fluid after its internal administration to infants. On contact with cerebro-spinal fluid at 37 to 38° C. the preparation gives off formaldehyde. Hence there is a possibility of a disinfectant action even in the living organism. It is said that an action of this kind may be demonstrated in the cerebro-spinal fluid to a slight extent after therapeutic doses. Ibrahim considers it advisable, for this reason, to try urotropine in all forms of serous and purulent meningitis. In infants and small children the author considers a dose of 0.75 to 1.5 gramme (12—24 grains) daily to be harmless, even on prolonged use.

### Valisan.

Valisan is the monobromo-isovalerianic ester of borneol, a clear fluid, like water, of the consistency of glycerin; it contains 25.2 p.c. of bromine, 26 p.c. of isovalerianic acid and 48 p.c. of borneol. It is issued in gelatin capsules containing 0.25 gramme each\*). Th. Kuttner has used the preparation with success in numerous cases in various disturbances of the central and sympathetic nervous systems. He found it of specially good service in neurasthenia, hysteria, irritability of the nervous system and neuroses accompanied

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Crowe, Merck's Reports 1909, p. 341.

Stockmayer, Allgemeine Wiener medizinische Zeitung 1910, No. 4 and 5.

Ibrahim, Medizinische Klinik 1910, No. 48.

\*) In use in America under the protected name of "Brovalol".  
Kuttner, Therapie der Gegenwart 1910, No. 8, p. 377.



with fear, in onanism and in Graves' disease, in climacteric troubles and in the conditions following hysterectomy with castration. In gastric neuroses with nausea and vomiting, and in hyperemesis gravidarum it is also of good service. In these cases 2 to 3 valisan capsules are given before rising in the morning, with a cup of black coffee not too hot. Two capsules 3 times a day are said to be useful in sea-sickness.

### Veratrine.

The internal administration of veratrine is usually avoided nowadays, though homœopaths still make use of the remedy in the treatment of diarrhœa and vomiting. In large doses the preparation causes diarrhœa and vomiting, in small doses it is said to be an efficacious remedy for these troubles. In feeble persons it is necessary to avoid its use, for it is said to be apt to cause collapse in such cases. G. Maetzke prescribed it with success in cholera nostras but believes it might be of good service also in Asiatic cholera. He prescribed the following mixture:

Rp. Veratrin.	0.005 gramme ( $\frac{1}{12}$ grain)
Spirit. dilut.	25.0 grammes ( $\frac{5}{6}$ oz)
Aq. destill.	ad 200.0 „ ( $6\frac{2}{3}$ oz)

One tablespoonful of this is given in four doses at intervals of half an hour and subsequently the same dose every two hours. The spirit contained in the mixture serves not only as a solvent for the veratrine, but also as an excitant. The usual dose, which was repeated several times a day, varies between 0.001 to 0.005 gramme ( $\frac{1}{64}$ — $\frac{1}{12}$  grain). Hence there is no need to fear the consequences of the small doses prescribed by Maetzke.

### Veronal and Veronal-Sodium.

In a pharmacological investigation as to its behaviour in the animal body when given once and when given repeatedly, C. Bachem came to the conclusion that small doses of veronal or of veronal-sodium after subcutaneous injection reappeared in the urine to the extent of about

Maetzke, Zeitschrift für ärztliche Fortbildung 1909, No. 22. —  
Deutsche Ärztezeitung 1910, No. 8.

Bachem, Archiv für experimentelle Pathologie und Pharmakologie 1910, Vol. 63, p. 228.

90 p.c. of the amount introduced, while large doses were only excreted to the amount of 45 to 50 p.c. The latter is the case not only with single large doses, but also after habituation to large quantities. But little veronal is eliminated in the fæces. It is probable, therefore, that when large doses of veronal are given, about half the amount is destroyed in the organism, though we do not know how this process occurs. It follows that the organism does not acquire the power of destroying veronal with time, as in the case of morphine. The author ascertained further that small doses repeated for long periods had scarcely any effect on the well-being of the animals. After three days but little veronal is to be found in the urine and in the single organs. Veronal shows a considerable affinity for the brain, and a sufficient hypnotic power is produced when the quantity in the brain amounts to 0.016 p.c. In other organs too, the presence of weighable amounts of veronal may be detected. When administered by mouth by far the greater quantity of the veronal leaves the stomach after a few hours. This justifies the assumption that acute poisoning with veronal, coming on after this period, can no longer be relieved by washing out the stomach. In cases of accidental or intentional veronal poisoning it will be best to follow W. Rosendorff's method of producing evacuation of the bowels and increased diuresis, and using excitants if need be.

The importance of veronal in psychiatric practice is increasing. This is shown by the communications of E. Wendt, Goering, E. von der Porten and F. Möller. Wendt tested the value of veronal as compared with sulphonal and methyl-sulphonal in the same individuals, in insane persons in a state of high excitability, and in varying degrees of sleeplessness. The external conditions were kept alike, the patients were in the same stage of disease and showed the same manifestations. His statistics show veronal to be superior to the two other remedies, though he believes that if allowance be made for coincidence, subjective peculiarities

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Rosendorff, *Berliner klinische Wochenschrift* 1910, No. 20, p. 934.

Wendt, *Therapeutische Monatshefte* 1910, No. 11, p. 599.

Goering, *Psychiatrisch-neurologische Wochenschrift* 1909, No. 24.

von der Porten, *Therapie der Gegenwart* 1910, No. 6, p. 270.

Möller, *Medische Revue* 1910, No. 8.

and errors of observation, sulphonal would be superior in the case of strong, lusty subjects of hallucination, and especially in cases of paranoia, while veronal-sodium would be preferable in the case of more feeble subjects, or in the presence of a bodily infirmity, as in paralytics and in senile subjects. The general character of the psychoses is not altered by veronal any more than by sulphonal or methylsulphonal. As regards the dosage, veronal-sodium, according to Goering, should not be given in doses of less than 1 gramme (15 grains) in conditions of severe excitation. This dose, however, secures a certainty of obtaining the desired effect in the majority of cases. Veronal-sodium is specially to be recommended in patients who take scopolamine frequently, or in those in whom scopolamine is contra-indicated, or at any rate its repeated use is contra-indicated. It is frequently of good service in such cases, and the patients are spared the constantly repeated administration of so powerful a poison as scopolamine. A further important circumstance is the fact that veronal, if it be refused when given *per os*, may be given subcutaneously. Goering does not think much of the disadvantage that 5 c. c. (85 min.) need to be injected for the purpose of administering 1 gramme (15 grains) of veronal-sodium subcutaneously. In such cases it is best to use a Pravaz syringe of 5 c. c. capacity. Veronal is of importance in the treatment of delirium tremens. Möller and von der Porten proved by their investigations that the preparation had a better effect on the course of delirium than bromine and chloral. It led to a diminished mortality, and prevented the appearance of the attack in many cases. The dosage was given in last year's Reports (1909).

It is now well known that veronal has become a popular hypnotic in long railway journeys. More recently it has been recommended for tourists who are frequently compelled to sacrifice refreshing sleep through fatigue or excitement. K. Blodig has found it a valuable remedy for those who visit the Alpine huts. He has used it personally for two years with excellent success, and has felt no unpleasant after-effects on the following morning. He found 1 gramme (15 grains) to be sufficient on the first day, and 0.5 gramme ( $7\frac{1}{2}$  grains) on the following days.

Blodig, Mitteilungen des Deutschen und Österreichischen Alpenvereins 1910, No. 10, p. 129.



E. Boesch has tried to treat labour pains with veronal-sodium when they were found to be too severe, either for objective or subjective reasons. He applied it rectally toward the end of the period of dilatation, in doses of 1 gramme (15 grains). In his experience the desired result sets in, as a rule, after 20 to 30 minutes. More effective is a combination of veronal (by mouth) with morphine (subcutaneously), for Bürgi, and more recently Homburger, have shown that this combination has a greater effect than we would be led to expect from the combined effects of the two remedies. M. Herz also found this combination of morphine and veronal of use in insomnia due to heart disease. If the usual cardiac tonics prove insufficient, a trial of morphine and veronal is justified and advisable.

Excellent results are also obtained with veronal in flatulence. Paffrath was unable to obtain as prompt an action with any other remedy, even with opium. Even in advanced cases with circulatory disturbances, where bromine, opiates, chloral hydrate and chloroform were of no use, veronal gave a satisfactory result. A disadvantage described by the author is the constipating action of veronal, though this rights itself as soon as the use of the drug is discontinued. He points out also that veronal has a beneficial action on the conjunctiva of the eye, and he recommends ophthalmologists to follow up this property.

The good results obtained by other authors with veronal in sea-sickness led Galler, Wolfram and Pauly to try it for this purpose. Galler found veronal-sodium to be better than veronal because it is more readily soluble, more rapidly absorbed, and hence acts more quickly. Further, its use enables the drug to be taken in solution with but little water, and this may be of some importance, since a large amount of liquid may favour a tendency to vomit. In long-continued rough weather the author gave 2 doses of

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Boesch, *Gynaecologia Helvetica* 1910, p. 327.

Bürgi, *Deutsche medizinische Wochenschrift* 1910, No. 1 and 2.

Homburger, *Deutsche medizinische Wochenschrift* 1910, No. 7.

Herz, *Pester medizinisch-chirurgische Presse* 1910, No. 40, p. 314.

Paffrath, communication in a letter.

Galler, *Therapie der Gegenwart* 1910, No. 2, p. 94.

Meyer, *Therapeutische Monatshefte* 1910, No. 6.

Wolfram, *Therapeutische Monatsberichte* 1910, No. 11.

Pauly, *Berliner klinische Wochenschrift* 1910, No. 11.

0.5 gramme ( $7\frac{1}{2}$  grains) of veronal-sodium within 24 hours. If the patient is able to retain the remedy for as long as ten minutes, Galler found that the patient may safely reckon on 12 hours' peace. In slight cases a single dose suffices. It is best given at night after retiring to bed. It is true the onset of sea-sickness cannot be prevented in every case, nor can the severe symptoms be relieved absolutely. There is no doubt, however, that veronal-sodium gives considerably relief from all the symptoms in the majority of cases, and consequently deserves to be strongly recommended as one of the best remedies for the treatment of sea-sickness. Regarding Galler's successful results, Wolfram\*) shows that veronal relieves the nausea which occasionally follows the use of morphine. Hence it is no coincidence that it relieves the nausea of sea-sickness. Further, Wolfram, unlike Galler, prefers veronal because its taste is less unpleasant than that of veronal-sodium. If it be not necessary to obtain the most rapid result possible, it may be left, in individual cases, to the taste of the sufferer from sea-sickness whether he prefers the one or the other. On the whole, good results will be obtained with both preparations. The results of Schepelmann are in accordance with the above conclusions. He reported on the treatment of sea-sickness with veronal years ago\*\*). There is as yet no prospect of preventing sea-sickness by the suitable construction of ships, hence we must endeavour, in the meantime, to subdue the sensitiveness of the central nervous organs to the ship's movements, and in Schepelmann's opinion this can best be done by the administration of veronal. A similar conclusion is arrived at by Pauly.

### **Yohimbin pro uso veterinario.**

A two-year-old pomeranian dog, whose hind paw had been lame for weeks so that it was compelled to stand on its forelegs while the hind part of its body lay on the ground, was treated by Löer with yohimbine tablets. After

\*) See *Ärztliche Mitteilungen* 1906, No. 28 and Merck's Reports 1906, p. 259.

Schepelmann, *Therapeutische Monatshefte* 1910, No. 12, p. 681.

\*\*) See Merck's Reports 1907, p. 254.

Löer, *Berliner tierärztliche Wochenschrift* 1910, p. 113.

eight days a marked improvement had set in, and after eight more days the animal was completely cured.

Hasack tried yohimbine in three bad milch cows which yielded no more than 2 to 5 litres of milk daily, but though the animals were given 0.1 gramme ( $1\frac{1}{2}$  grains) 3 times a day for more than a month, there was no appreciable increase in the yield of milk in any case. On the other hand there occurred a slight rise of temperature after the 8<sup>th</sup> and 10<sup>th</sup> day of treatment, the respiration and the pulse increased in frequency, and the external genitals showed swelling and fulness. Similar results have already been observed by others. In the case of two animals kept for breeding purposes, however, where there was deficient sexual desire, a completely successful result was obtained after 5 to 6 days' administration of yohimbine.

Wölffer refuses to attribute to yohimbine any action on the sexual desire of cows, for in two cases he had no success with the drug. To deny the utility of a drug that has been favourably reported on by many others merely on account of a single failure, is just as wrong as to give excessive praise as the result of a single success. For this reason Pfab is right in suggesting that a larger number of trials should be made before attempting to upset the opinion of other workers. His own experience with yohimbine in 79 animals is calculated to neutralise the over hasty warning of Wölffer against the use of yohimbine, for his report shows that in 78.5 p.c. of the cases treated by him a successful result was obtained. He used the preparation in the form of a solution. Large animals were given a tablespoonful 3 times a day of a mixture consisting of 0.5 gramme ( $7\frac{1}{2}$  grains) of yohimbine in 200 grammes ( $6\frac{2}{3}$  oz) of water, given in their food. Smaller animals (such as pigs) were given the same amount of a solution of 0.1:200.0. O. E. Vogel gave yohimbine internally to a horse and a cow, and reported a successful result in each case. He has less confidence in its subcutaneous use, and the same opinion has been expressed by others\*).

Hasack, Österreichische Monatsschrift für Tierheilkunde 1910, p. 97.

Wölffer, Berliner tierärztliche Wochenschrift 1910, p. 352.

Pfab, Berliner tierärztliche Wochenschrift 1910, p. 409.

Vogel, Berliner tierärztliche Wochenschrift 1910, p. 408.

\*) See Merck's Reports 1905, p. 221.



The title of this article indicates that I issue for veterinary purposes a yohimbin pro uso veterinario. To prevent any misunderstanding I would remark that this preparation is just as efficacious as pure yohimbine. It is necessary, however, to give it in double the dose, for "yohimbin pro uso veterinario" contains only 50 p.c. of yohimbine hydrochloride. This step was taken to enable yohimbine to be sold at a lower price for veterinary use, in which far larger doses are given than for use in human medicine. I issue the following preparations for veterinary purposes:

Yohimbin. hydrochlor. ad usum veterinarium. It contains 50 p.c. of pure yohimbine hydrochloride.

Yohimbine tablets ad usum veterinarium (coloured grey) each containing 0.01 gramme ( $\frac{1}{6}$  grain) of yohimbine hydrochloride, and

Yohimbine tablets ad usum veterinarium (coloured red) containing 0.1 gramme ( $1\frac{1}{2}$  grains) of yohimbine hydrochloride.

Hence each tablet, in addition to the vehicle, contains the full dose of yohimbine hydrochloride stated above (usually briefly called yohimbine). This explanation is rendered necessary by a technical paper on commercial preparations in which doubts have been expressed on this point. My yohimbine preparations and tablets are accurately labelled and dosed; they are coloured in the manner described above, and I am prepared to give a full guarantee that they contain the amount stated.

### **Zinci acetat.**

A new reagent for urobilin, urobilinogen and blood has been described by A. Florence. Fundamentally it consists of nothing more than a combination of Roman-Delluc's test for urobilin and Donogany's and Wolff's test for blood\*). It is prepared by dissolving 7.5 grammes of zinc acetate in 50 grammes of alcohol, and adding to this solution 50 grammes of pyridine and 50 grammes of chloroform. To carry out the test, 2 to 3 c.c. of the urine to be tested are taken, double the quantity of the reagent is added,

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Florence, Journal de pharmacie et de chimie 1910, II, p. 160. —  
Répertoire de pharmacie 1910, No. 10, p. 447.

\*) See Merck's Reagenzien-Verzeichnis 1908.

and the mixture is shaken. An emulsion is thus formed; this separates into two layers. In the presence of urobilin the lower layer shows a green fluorescence. If the latter does not occur until the mixture has stood for a time, this points to the presence of urobilinogen. If a greenish colour appears first, and then a fluorescence, this points to bilirubin. In the presence of blood a pink to cherry-red colour appears. The solution may also be tested for the characteristic absorption spectra, and the author states that with the use of the method above described they are very distinctly recognisable. The reaction has the advantage of being applicable without special manipulations such as clearing and filtering the urine to be tested.

### **Zinci sulphas.**

A communication by Ganassini shows zinc sulphate to be a very sensitive test for uric acid, and by using it the well known murexide reaction may be dispensed with. If an aqueous solution of zinc sulphate be added to a solution of uric acid, or of an alkaline urate, a white, basic urate of zinc separates out. On exposure to air it is said to assume gradually a greenish or blue colour. This reaction is not affected by the presence of albumens, hence it may be used for the detection of uric acid in blood.

### **Zinc Eucerin Gelanth.**

For the treatment of intertrigo in children, P. G. Unna recommends a mixture consisting of 50 grammes ( $1\frac{2}{3}$  oz) of zinc oxide, 25 grammes ( $\frac{5}{6}$  oz) of eucerin and 25 grammes ( $\frac{5}{6}$  oz) of gelanth\*). It forms a soft, white mass which is easily rubbed into the skin, has an agreeable cooling effect and dries rapidly. The addition of eucerin renders gelanth, which contains water, fatty and smooth so that when it dries it does not form too hard a layer upon the skin. To make this layer insoluble in water so that it is not washed away

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Ganassini, *Revue pharmaceutique des Flandres* 1909, p. 361. — *Nouveaux remèdes* 1909, p. 39. — *Apotheker-Zeitung* 1910, p. 38.

Unna, *Monatshefte für praktische Dermatologie* 1910, Vol. 50, p. 300.

\*) Gelanth is a mixture of tragacanth, superheated gelatin glycerin and water.

too rapidly when it becomes moist, this so-called zinc varnish is covered with a mixture of equal parts of tannic acid and magnesium carbonate. The various substances now react upon one another with the result that zinc tannate is formed, and the gelanth and tannin form a tough, elastic mass. Moreover the tannic acid is gradually oxidised by the influence of the basic substances, an unknown body being formed which may possibly assist the curative action of the ointment mixture. The treatment has the advantage that children suffering from eczema intertrigo do not require to be dried more frequently than other children. The napkins may be changed several times as a rule without displacing the varnish, and the varnish does not require to be renewed until it comes off. Under it the eczema heals fairly rapidly, for it has a curative effect while it protects the skin from becoming moistened with urine. For this reason the varnish may also be of good service in bedsores.

### Zincopyrin.

Zincopyrin is phenyl-dimethyl-pyrazolone zinc chloride, a compound of the composition  $(C_{11}H_{12}N_2O)_2ZnCl_2$ . It was first prepared and described by Schuyten. It forms shining scales that melt at  $156^{\circ}C$ . In cold water it dissolves to about 5 p.c., in hot water to about 12 p.c. It is readily soluble in dilute alcohol and in chloroform.

The use of zincopyrin was suggested by E. Boesch in the place of the 5 p.c. chloride of zinc paste for the treatment of inoperable carcinoma of the uterus. It has the advantage of having less caustic action than chloride of zinc; hence there is less danger of toxic action than when pure chloride of zinc is used. The antipyrine component of the preparation has the effect of diminishing the pain caused by the caustic. Boesch has described the following method: The carcinomatous parts are thoroughly scraped and plugged with xeroform gauze to prevent severe hæmorrhage. After 24 hours the plugs are removed, when the edges of the wound begin to granulate. After about 8 days a small quantity of zincopyrin is applied in the form of 40 p.c. zincopyrin gauze. In doing this, care must be taken to plug the entire

Schuyten, *Chemiker-Zeitung* 1895, p. 1421.

Boesch, *Korrespondenzblatt für Schweizer Ärzte* 1910, No. 2.



wound cavity and no more, otherwise healthy tissues may be subjected to the caustic action. A few pledgets of wool are placed upon the plugs; they keep the plug in position and absorb the discharge as it escapes. Otherwise it might injure the vulva and perineum. If the plug has been applied skilfully no pain is produced. It is removed after 12 or 24 hours, according as to whether the tampon lies near the bladder or bowel, or there is a thick intervening wall. The patient remains in bed. A white crust forms and separates after some days, leaving a cavity with good granulations. The discharge diminishes, the hæmorrhage ceases and the foul smell disappears. After 10 to 14 days this treatment is repeated. It produces improvement of fairly long duration, and gives the patient new hope.

### **Zinc-Perhydrol.**

In the treatment of soft sores, zinc-perhydrol was found by Müllern-Aspegren to be of excellent service, having special advantages over the usual powders applied in dry treatment. The author begins by attempting to convert the virulent ulcer into an non-virulent one by the application of chloride of zinc. He then covers it with a thick layer of zinc-perhydrol. If necessary cotton wool is applied over it and fixed with a bandage. The further treatment can, as a rule, be carried out by the patient himself. He cleanses the ulcer three times a day with an antiseptic solution, and then applies zinc-perhydrol. In case it should become virulent again, the physician must apply the caustic once more. On using zinc-perhydrol the author found that the ulcer became clean sooner than when iodoformogen, euophen and calomel were used. Hence he considers zinc-perhydrol superior to the iodoform substitutes, and this is all the more important in view of the complete freedom from smell of the preparation, and its deodorizing action. Moreover zinc-perhydrol is colourless and produces no irritant effects.

H. Klute has recently shown by animal experiments that zinc-perhydrol, when used therapeutically, combines the antiseptic action of the oxygen which is set free with the astringent action of the zinc oxide. It is a very useful anti-

septic and astringent, it dries wounds, limits suppuration, and promotes granulation. For this reason it is indicated in surgical diseases in which there is copious formation of pus, for example in infected wounds and suppurating inflammation of the skin and mucous membrane.

Ch. W. Hancken recommends the following prescriptions for the treatment of wounds, ulcers, cellulitis and skin affections:

Rp. Zinc-perhydrol	25.0	grammes ( $\frac{5}{6}$ oz)
Vaselin. alb.	75.0—100.0	„ ( $2\frac{1}{2}$ — $3\frac{1}{3}$ oz)
	or	
Rp. Zinc-perhydrol	50.0	grammes ( $1\frac{2}{3}$ oz)
Talc. Venet.	150.0	„ (5 oz)

Hancken states that in using these prescriptions the practitioner will have no reason to complain of unwelcome occurrences.

Werner has used zinc-perhydrol as well as perhydrol in the treatment of wounds of the cornea, and inflammation of the conjunctiva of the eyelids of horses, and he has obtained very satisfactory results. He always used it in the form of a powder, for in spite of its granular character, it may be applied in this form by insufflation to the conjunctiva without producing the least untoward consequences. Werner found that it reduced the inflammation more rapidly than any other remedy. Even severe swelling of the lids with purulent discharge is said to subside in a short time.

### Milk poor in sugar.

This is prepared for diabetics and for gastric and intestinal cases according to the directions of Schottelius and E. Lampé. It is issued by the Natura Milk Export Company, Bosch & Co., Waren (Mecklenburg). The milk is supplied ready for use, sterilised and rendered homogeneous, hence it keeps indefinitely. It is issued in tins containing about half a litre.

That there is a demand for a preparation of this kind is shown by the publications, during the past year, of H.

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Hancken, Berliner tierärztliche Wochenschrift 1910, No. 49.  
Werner, Zeitschrift für Veterinärkunde 1910, No. 7.

Finkelstein and Meyer, Petruschky, J. Braumüller, H. Lehdorff and E. Zak. They do not deal specially with Lampé-Schottelius's milk, though they draw attention to the value of a sugar-free milk diet, and the value of trustworthy sterilised "stable" milk preparations, particularly in the gastric and intestinal diseases of infants.

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Finkelstein-Meyer, Über Eiweissmilch. Ein Beitrag zum Problem der künstlichen Ernährung. Jahrbuch für Kinderheilkunde 1910, p. 525 and 683.

Petruschky, Richtlinien zur Bekämpfung der Sommersterblichkeit der Säuglinge. 82<sup>nd</sup> Naturforscher-Versammlung in Königsberg. Monatsschrift für Kinderheilkunde 1910, No. 6, p. 252.

Braumüller, Über toxische Zuckerwirkung. Münchener medizinische Wochenschrift 1910, No. 49, p. 2571.

Lehdorff-Zak, Über dialysierte Milch. Wiener medizinische Wochenschrift 1910, p. 1930.

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## Index of Authors.

	Page
Abderhalden, E. . . . .	145
Abraham, O. . . . .	180
Adam . . . . .	235
Adam, C. . . . .	169
Adler, O. . . . .	362
Albrecht, H. . . . .	103
Aldor, L. v. . . . .	192
Alexander, A. . . . .	359
Alister, J. Mc. . . . .	182
Allard . . . . .	19
Alt, K. . . . .	309. 313. 316
Alvarez Sainz de Aja . . . . .	319
Amako, T. . . . .	299
Ammon, v. . . . .	210
Anelli, L. . . . .	22
Annoni . . . . .	2
Anscherlik, H. . . . .	311
Ardell, M. . . . .	188
Arlt, B. R. v. . . . .	363
Arning . . . . .	315
Arnold, W. J. J. . . . .	260
Arnsperger, H. . . . .	192
Asch, R. . . . .	231. 353
Ascher, J. . . . .	148
Assmy, H. . . . .	316
Astruc . . . . .	6. 33
Auburg . . . . .	126
Aufrecht . . . . .	126
Auger . . . . .	34
Azua, J. de . . . . .	116
Bachem, C. . . . .	369
Badel . . . . .	6
Baer . . . . .	125
Balzer . . . . .	28
Balzer, F. . . . .	203
Bang . . . . .	302

	Page
Barabaschi, P. . . . .	188
Barbano, E. . . . .	29
Barbary . . . . .	32
Barbier, P. . . . .	171
Bardach, B. . . . .	348
Bardachzi, F. . . . .	315
Bardet . . . . .	314
Barile, C. . . . .	94
Barth . . . . .	16
Barthe . . . . .	2. 6
Baruch, M. . . . .	101
Baty . . . . .	196
Baudisch . . . . .	152
Bauer . . . . .	315
Baugh . . . . .	329
Baum, E. W. . . . .	219
Bäumer, E. . . . .	112. 113. 291
Baumgarten, E. . . . .	151
Baurowicz, A. . . . .	280
Bausenbach . . . . .	184
Bayer, H. . . . .	235
Bayet, A. . . . .	314. 316. 319
Bayeux . . . . .	14
Beard . . . . .	366
Beck, C. . . . .	123
Beck, E. G. . . . .	123
Beck, O. . . . .	314
Becker, F. . . . .	288
Beebe . . . . .	67
Beer, C. . . . .	324
Beitzke, H. . . . .	94
Bell, W. B. . . . .	269
Belohubek . . . . .	321
Bender . . . . .	311
Berard . . . . .	219
Berendes . . . . .	194
Berg, J. . . . .	219

	Page
Bergel, S. . . . .	354
Berger, H. J. . . . .	198. 354
Bergien, W. . . . .	274
Bergrath, R. . . . .	118. 296
Berliner, L. . . . .	294
Berliner, M. . . . .	144
Berlioz . . . . .	33
Bermann, E. . . . .	130
Berri, C. . . . .	160
Bertarelli . . . . .	319
Bertherand . . . . .	21
Bertrand . . . . .	321
Bethge, H. . . . .	280
Beurmannn . . . . .	316
Beyer . . . . .	278. 331
Beyerinck, W. . . . .	42
Biach . . . . .	319
Bial . . . . .	261
Bianchi, A. . . . .	165
Biehler, M. de . . . . .	6
Biel . . . . .	46
Bielow, N. A. . . . .	262
Bierotte, E. . . . .	94
Bilinskis, L. . . . .	130. 131
Billet, H. . . . .	16. 20
Biltz, H. . . . .	152
Birch-Hirschfeld, A. . . . .	116
Bircher, E. . . . .	124. 238. 263. 266
Bissauge, R. . . . .	220
Bittner, J. . . . .	301
Blaikie, R. H. . . . .	114
Blanchard . . . . .	124
Blaschko . . . . .	310
Blessing, G. . . . .	276
Bloch, C. E. . . . .	321. 324
Blodig, K. . . . .	371
Bloemendal . . . . .	6
Blondel . . . . .	321
Blumenfeld, A. . . . .	313
Blumenthal, F. . . . .	261. 340
Blumm, R. . . . .	287
Boberg, J. . . . .	279
Bochberg . . . . .	116
Böcker . . . . .	320
Boehringer . . . . .	99
Boeßer . . . . .	148
Boesch, E. . . . .	372. 377
Boethke, O. . . . .	117

	Page
Bogdán, A. . . . .	220
Bohac, K. . . . .	309. 318
Bolognesi . . . . .	37
Bondy, O. . . . .	223
Bonhöfer . . . . .	312
Bönning, F. . . . .	227
Bonsignorio . . . . .	27. 37
Boos, W. F. . . . .	160
Borchers, H. . . . .	109
Bordas, F. . . . .	122
Borde . . . . .	95
Bormann, S. . . . .	311. 317
Bormans, A. . . . .	24
Bosse, B. . . . .	326
Bottelli . . . . .	319
Bougault . . . . .	6. 95
Bourlier . . . . .	304
Bradt, G. . . . .	222
Braendle, E. . . . .	136. 310
Braga, A. . . . .	184
Braitmaier . . . . .	150
Brandenburg, F. . . . .	182
Brandes . . . . .	124
Braun . . . . .	220
Breuer . . . . .	105
Brewitt, R. . . . .	219
Brimont . . . . .	197
Brocq . . . . .	3. 14. 33
Broers . . . . .	55
Bröking, E. . . . .	223. 227
Bruch, F. . . . .	217
Bruck, C. . . . .	331
Bruck, F. . . . .	149
Brühl . . . . .	192
Bruhns, C. . . . .	317
Brunet . . . . .	28
Brüning . . . . .	237. 259
Brüning, A. . . . .	79. 365
Brüstlein, G. . . . .	274
Bubenhofer, A. . . . .	89
Buchholz, A. . . . .	188
Buck . . . . .	176
Buck, Ch. S. . . . .	99
Bufalini, G. . . . .	176
Buß . . . . .	224
Bunsen . . . . .	1. 4
Bünthe, H. . . . .	257
Buob . . . . .	278

	Page
Bürck . . . . .	41
Bürgi . . . . .	130. 327. 372
Burkhardt . . . . .	78
Burlureaux . . . . .	20. 32. 35
Burman . . . . .	159
Burow . . . . .	337
Burow, R. . . . .	200
Burri, R. . . . .	218
Busch, Ch. . . . .	235
Buschke, A. . . . .	314
Busse . . . . .	316
Butenko, A. . . . .	213
Cadet . . . . .	1
Callivokas, A. . . . .	128
Campana, R. . . . .	312. 318
Campbell . . . . .	321
Campbell, Mc. . . . .	296
Camus, J. . . . .	319
Camus, L. . . . .	319
Canal . . . . .	264
Candela y Pla . . . . .	71
Canestro, C. . . . .	243
Cantani, A. . . . .	292
Carlson . . . . .	6
Carrion . . . . .	48. 50
Carteret . . . . .	63
Caspars . . . . .	151
Castelli, G. . . . .	186
Caussade . . . . .	149
Cavalié . . . . .	276
Cavazzani, A. . . . .	189
Cerletti . . . . .	268
Championnière . . . . .	221
Chandet . . . . .	189
Chantemesse . . . . .	70
Chassevant . . . . .	37
Chattot . . . . .	219
Chauffard . . . . .	149
Chaumier . . . . .	37
Chavanne, F. . . . .	297
Cheinnisse . . . . .	84
Chevalier, J. . . . .	144
Chiappori . . . . .	6. 25
Chiari, R. . . . .	133
Chibret . . . . .	242
Chiray . . . . .	316
Chlapowski, F. v. . . . .	345

	Page
Cholewa . . . . .	283
Chomse . . . . .	4
Christopher-Crofton . . . . .	302
Chrzelitzer . . . . .	291. 316
Ciavette . . . . .	34
Citron, H. . . . .	312. 313
Ciuffi, G. . . . .	202
Clairmont . . . . .	79
Clifford . . . . .	324
Clingestein . . . . .	310
Cocco, L. . . . .	201
Cochez . . . . .	37
Cohn . . . . .	126
Cohn, P. . . . .	233. 312
Collet . . . . .	19
Collins, U. . . . .	324
Comby . . . . .	268
Conseil . . . . .	314
Corin, J. . . . .	163
Corrado, C. . . . .	243
Cracken, Mc. . . . .	87
Cremer . . . . .	326
Crescenzi, G. . . . .	143
Crismer . . . . .	302
Croner . . . . .	277
Crowe . . . . .	368
Cukor, N. . . . .	68
Dabbs, G. H. R. . . . .	353
Dalché . . . . .	20
Dale . . . . .	328
Damaye . . . . .	270
Daniel, G. . . . .	224
Daniel, J. . . . .	350
Danielopolu . . . . .	352
Danlos . . . . .	9. 10. 21
Darré, H. . . . .	315
Dawes, L. . . . .	6. 344
Daxenberger, F. . . . .	104. 249. 278
Delbet, P. . . . .	140. 291
Denarié, A. . . . .	303
Denk, W. . . . .	79
Desmoulière . . . . .	209
Devic . . . . .	329
Deycke, G. . . . .	252. 253
Dianoux . . . . .	178
Dienst, A. . . . .	207
Diesing . . . . .	77



	Page
Dietrich . . . . .	277
Dietrich, G. J. . . . .	132
Dietrich, W. . . . .	117
Dillon, J. . . . .	183
Dimitrieff . . . . .	39. 41
Dixon Mann . . . . .	195
Dmitrenko, L. Ph. . . . .	172
Doberer, J. . . . .	157
Dobrovits . . . . .	311
Döderlein . . . . .	68
Dohi . . . . .	313
Dohrn, M. . . . .	272
Dölling, M. . . . .	235
Dollinger . . . . .	124
Domerkinowa . . . . .	319
Donagh, Mc. . . . .	311
Donald, E. Mc. . . . .	262
Donati, M. . . . .	220
Don . . . . .	124
Donath, J. . . . .	69
Dörbeck, F. . . . .	334
Dössekker, W. . . . .	313
Dresler . . . . .	50. 53. 61
Dreuw . . . . .	147. 215
Dreyer, W. . . . .	289
Duhot, R. . . . .	310. 311. 313
Dujardin . . . . .	315
Dumont, J. . . . .	313
Dungern, v. . . . .	341
Dupont, R. . . . .	140
Dürr . . . . .	279
Dutoit . . . . .	169
Ebermann . . . . .	278
Eckard . . . . .	109
Eckermann . . . . .	214
Eckervogt . . . . .	45. 48
Edelen, Ch. A. . . . .	92
Eggenberger . . . . .	124
Ehlers . . . . .	312. 313
Ehrlich, P. . . . .	308. 312. 318. 319.
Ehrmann, O. . . . .	175
Ehrmann, R. . . . .	253
Ehrmann, S. . . . .	311
Eichhorst, H. . . . .	289
Eichler . . . . .	273
Eisenberg, J. . . . .	43
Eisenstein, J. . . . .	66

	Page
Eisert . . . . .	89
Eitner, E. . . . .	310. 315
Elbe . . . . .	124
Elias, H. . . . .	346
Eliasberg, W. . . . .	326
Elsner, H. J. . . . .	318
Emery . . . . .	313. 317. 319
Engelmann, F. . . . .	207
Engelmann, W. . . . .	191
Engstad, J. E. . . . .	81
Erdös . . . . .	88. 119
Erlandsen . . . . .	151
Escherich . . . . .	315
Evoli . . . . .	19
Ewald, C. A. . . . .	275
Ewan, D. Mc. . . . .	234
Ewart, W. . . . .	16. 20. 24. 25
Ewins, A. J. . . . .	77
Exner . . . . .	75
Eysselt von Klimpély, A. . . . .	267
Eysseric . . . . .	36
Fabri, E. . . . .	71
Fabry, J. . . . .	241. 317
Falk, E. . . . .	136
Falkenstein . . . . .	67
Falta, W. . . . .	75
Fausser, A. . . . .	315
Faust, E. St. . . . .	195
Faust, J. . . . .	324
Favento . . . . .	312
Federmann . . . . .	219
Fedoroff, S. P. . . . .	205
Feig . . . . .	49
Fein . . . . .	319
Fickler, A. . . . .	216
Fieber, E. L. . . . .	259
Fildes . . . . .	318. 319
Finckh, J. . . . .	74
Finger . . . . .	317
Fink, J. . . . .	287
Fiora . . . . .	30
Fiori, L. . . . .	183
Fischer . . . . .	126. 279. 319
Fischer, B. . . . .	317
Fischer, H. . . . .	91
Fischer, Ph. . . . .	309
Fischer, W. . . . .	314

	Page
Flatau, G. . . . .	202
Fleckseder, R. . . . .	143. 311. 315
Fleig, C. . . . .	189. 209
Fleißig, P. . . . .	89
Fleischmann, P. . . . .	74
Flemming, P. . . . .	311
Fleroff . . . . .	49
Flexner, S. . . . .	281
Fließ, W. . . . .	266
Florence, A. . . . .	375
Focke . . . . .	157
Fontoynt . . . . .	37
Forbát . . . . .	313
Forconi, G. . . . .	320
Fordyce . . . . .	314
Fordyce, J. A. . . . .	315. 316
Forschbach, J. . . . .	271
Forster . . . . .	55
Forster, F. v. . . . .	259
Fortunati . . . . .	71
Fourmestraux . . . . .	124
Fraenkel, C. . . . .	310
Fragola, V. . . . .	301
Franck, E. . . . .	31
Fraisse . . . . .	34
Franchini, G. . . . .	268
Frank . . . . .	221. 224
Frankl-Hochwart, L. v. . . . .	269
Fränkel, C. . . . .	173
Franze, P. C. . . . .	158
Franzen, J. . . . .	161
Fraser . . . . .	344
Fraser, Th. R. . . . .	5
Frenkel . . . . .	315
Frerich . . . . .	99
Fresenius, R. . . . .	153
Freudenreich, E. v. . . . .	44
Freund . . . . .	310
Frey . . . . .	126
Fried, A. . . . .	171
Friedenwald . . . . .	321
Friedländer, M. . . . .	313
Friedländer, W. . . . .	187
Friedmann . . . . .	228
Froehlich . . . . .	300
Fröhlich, A. . . . .	148. 269
Fröhner . . . . .	111
Fromme . . . . .	93

	Page
Frühwald . . . . .	343
Fuchs . . . . .	278
Fürth, J. . . . .	314
Gabrilowitsch . . . . .	339
Galatti . . . . .	127
Galewski . . . . .	317
Galewsky . . . . .	315
Galezowski . . . . .	27
Galler . . . . .	342
Gallo . . . . .	37
Gallois, P. . . . .	20. 23
Ganassini . . . . .	6. 376
Gandini, V. . . . .	188
Garand . . . . .	25
Garbat, A. L. . . . .	339
Gardère . . . . .	329
Gastou . . . . .	14
Gaucher . . . . .	14. 315
Gaudier . . . . .	323
Gautier . . . . .	9. 17. 27. 28. 29. 37
Gazzetti . . . . .	72
Gebhard . . . . .	48
Gellhorn . . . . .	64
Gennerich . . . . .	311. 319
Genty . . . . .	119
Georgiewski, K. . . . .	39. 109
Georgii . . . . .	126
Gerber, B. . . . .	259. 316. 318
Gergö . . . . .	327
Géronne, A. . . . .	311. 317
Giani . . . . .	142
Gijselmans, H. . . . .	12
Gilbert . . . . .	29
Gilmour, J. R. . . . .	329
Gioseffi, M. . . . .	316
Giuffo . . . . .	33
Glaas, J. . . . .	188
Glass . . . . .	318
Glässner, K. . . . .	345
Glück, A. . . . .	312. 313
Gockel . . . . .	259
Goering . . . . .	370
Goldbach . . . . .	317
Goldhausen . . . . .	39
Goldschmidt, A. . . . .	177
Goldschmidt, G. . . . .	252
Golodetz, L. . . . .	146. 366

	Page
Golopp . . . . .	277
Göppert, F. . . . .	335
Gordon . . . . .	339
Görges . . . . .	232
Görner . . . . .	126
Görres . . . . .	94
Gottheil, W. S. . . . .	240
Gotthilf . . . . .	277
Gourwitsch, M. . . . .	311
Gräfenberg . . . . .	275
Graff, E. v. . . . .	70
Gramenitzki, Th. . . . .	104
Graßmann, K. . . . .	313
Gratkowski, S. v. . . . .	350
Grau, H. . . . .	190
Greeff, J. H. . . . .	122
Green, W. D. . . . .	4
Green, W. O. . . . .	296
Grekow, J. . . . .	220
Greve . . . . .	278
Greven, K. . . . .	312
Grieve, J. . . . .	41
Griffon . . . . .	28
Grimm . . . . .	144
Grön, K. . . . .	250
Gros, O. . . . .	256
Groß . . . . .	318
Groß, E. . . . .	257
Groß, E. v. . . . .	311
Grossich . . . . .	219
Großmann, F. . . . .	91
Grothe . . . . .	127
Grouven, C. . . . .	310. 313
Grünbaum . . . . .	350
Grünbaum, C. . . . .	249
Grünfeld, A. J. . . . .	313. 319
Guelpa . . . . .	319
Guérin . . . . .	37
Gumbert, E. . . . .	228
Günther, H. . . . .	246
Güntz, J. E. . . . .	286
Gurwitsch . . . . .	317
Guttmann, V. . . . .	293
Haagner, L. . . . .	201
Haberlandt . . . . .	320
Halberstädter . . . . .	298
Hale, W. . . . .	161

	Page
Haller . . . . .	319
Hallervorden, J. . . . .	275
Hallion . . . . .	48. 50
Hallopeau, H. . . . .	204. 314
Hamm . . . . .	89
Hammer . . . . .	314
Hammes, F. . . . .	109
Hanausek . . . . .	320
Hancken, Ch. W. . . . .	379
Hannes, W. . . . .	237
Hanus, J. . . . .	152
Harnack . . . . .	99
Harris, W. . . . .	85
Hart, C. . . . .	264
Hartmann . . . . .	312
Hartmann, E. . . . .	256
Hartung . . . . .	312
Harz . . . . .	321
Hasack . . . . .	374
Hasselbalch . . . . .	301
Hata, S. . . . .	308
Hatzfeld, A. . . . .	293
Hauckold, E. . . . .	327
Hausmann, Th. . . . .	316. 318
Havas . . . . .	318
Hayem . . . . .	50
Haymann, H. . . . .	275
Hayn, F. . . . .	187
Hayward . . . . .	91
Hecht . . . . .	316
Hecker . . . . .	55. 316
Heeger, F. . . . .	181
Heffter . . . . .	5. 6
Heiden . . . . .	315
Heilig . . . . .	290
Heimann, F. . . . .	275
Heinicke . . . . .	132
Heinrich . . . . .	110
Heinz, O. . . . .	363
Heitler, M. . . . .	149
Helblig . . . . .	286
Henle . . . . .	273
Hentrich . . . . .	225
Herff, O. v. . . . .	222. 349
Hering, H. E. . . . .	318
Herrenknecht . . . . .	276
Hertzler . . . . .	296
Hersheimer, K. . . . .	310



	Page		Page
Herz . . . . .	43	Intosh, Mc. . . . .	311. 319
Herz, M. . . . .	372	Isaac, H. . . . .	310
Herzfeld, E. . . . .	252	Ivanyi, M. . . . .	313
Hesky . . . . .	292	Ivcovic, L. . . . .	75
Hesse, C. . . . .	220	Iversen, J. . . . .	109. 309. 313
Hesse . . . . .	237		
Heubner, W. . . . .	310. 338	Jackson, C. . . . .	344
Heusner . . . . .	123	Jackson, G. T. . . . .	296
Heußner . . . . .	221	Jacob, L. . . . .	293
Hilbert . . . . .	367	Jacquet . . . . .	313. 315
Hippel . . . . .	146	Jadassohn . . . . .	318
Hirsch . . . . .	50. 54. 316. 338	Jaenecke . . . . .	382
Hirsch, M. . . . .	238	Jakimow . . . . .	319
Hirschberg . . . . .	239	Jakowlew . . . . .	319
Hirschberg, A. . . . .	97	Jaksch . . . . .	193
Hirschel, G. . . . .	135	Jalaguier, A. . . . .	16
Hirschfeld . . . . .	341	Jamieson . . . . .	332
Hirschmann, L. J. . . . .	296	Janssen, P. . . . .	78
Hirth, F. . . . .	176	Januschke, H. . . . .	75. 133
Hochsinger . . . . .	182	Jarusow, S. . . . .	115
Hödtke, O. . . . .	152	Jarvis, C. . . . .	332
Hofbauer, J. . . . .	292	Jeanselme . . . . .	313. 315
Hoffmann, E. . . . .	310	Jefimow, J. . . . .	213
Hoffmann, K. F. . . . .	112	Jenssen, F. . . . .	107
Hohn . . . . .	138	Jessner . . . . .	214. 317
Höhne . . . . .	135	Joachim, G. . . . .	199
Holmboe, O. . . . .	120	Jochheim, Ph. . . . .	7. 18
Holländer, H. . . . .	86	Jochmann, G. . . . .	339
Holst, M. . . . .	279	Johnson, E. . . . .	243
Homburger . . . . .	372	Jordan, A. . . . .	314. 316
Höpfel . . . . .	126	Joseph, M. . . . .	313. 358
Hoppe, J. . . . .	309. 316	Josephsohn . . . . .	131
Horand . . . . .	86	Josué . . . . .	253
Horn . . . . .	127	Jourdan . . . . .	88
Horton, H. E. L. . . . .	258	Juliusberg, F. . . . .	313
Houdard . . . . .	197	Jullien . . . . .	33
Howard, H. C. . . . .	183	Junkermann, K. . . . .	310
Hügel, G. . . . .	312	Jüsgen . . . . .	290
Hunt . . . . .	266	Justmann . . . . .	297
Hutschenreiter, K. . . . .	77		
Hyndham, H. F. . . . .	245	Kahn, J. . . . .	173
		Kaiser, R. . . . .	68
Ibrahim, J. . . . .	368	Kalb, R. . . . .	312
Igersheimer, J. . . . .	318	Karrick, A. . . . .	39
Ikada, T. . . . .	142	Katholicky, R. . . . .	259
Imbert . . . . .	6	Katz, W. . . . .	91
Impens, E. . . . .	73	Kaufmann, B. . . . .	175
Impens . . . . .	153	Kaufmann, L. . . . .	358

	Page
Kausch, W. . . . .	194. 220
Kellas-Wethered . . . . .	302
Kellerhals, H. . . . .	286
Kellner . . . . .	321
Kennard, D. . . . .	241
Kepinow . . . . .	343
Kern, E. . . . .	42
Kisch . . . . .	39
Kitao . . . . .	321
Klausner, E. . . . .	315. 316
Klebs, E. . . . .	94
Klein, W. . . . .	350
Klinger, B. . . . .	13
Klingmüller . . . . .	204
Klose . . . . .	265
Klotz . . . . .	61. 128. 241
Klute, H. . . . .	378
Knauer, R. . . . .	314
Knoke . . . . .	219
Knorr, R. . . . .	361
Kobert, . . . . .	43. 52. 54. 286. 239
Kobler . . . . .	315
Koch, W. . . . .	249
Kock . . . . .	19
Koelsch . . . . .	331
Koerner, B. . . . .	255
Kohan, M. . . . .	208
Kohl . . . . .	319
Kohlbach, O. . . . .	303
Köhler, C. . . . .	84
Kolossow . . . . .	199
König, J. . . . .	45
Königstein, H. . . . .	313
Konrad, E. . . . .	142
Kontschalowski . . . . .	351
Korczynski, L. K. v. . . . .	313
Koslow . . . . .	94
Köster . . . . .	323
Kowalewski . . . . .	316
Kownatzki . . . . .	76
Kraatz, A. . . . .	257
Krakauer . . . . .	39
Kranzfeld . . . . .	109
Kraus, F. . . . .	338
Krawkoff . . . . .	206
Krebs, G. . . . .	316
Kren, O. . . . .	316
Kretz . . . . .	326

	Page
Kromayer . . . . .	310. 317
Krösing . . . . .	314
Krüger . . . . .	94
Kucera . . . . .	105
Kühne . . . . .	94
Kukay, G. . . . .	279
Kulnew . . . . .	319
Külz, L. . . . .	145
Kümmell . . . . .	235. 324
Kuntsschik, F. . . . .	282
Kürschner . . . . .	4
Küster . . . . .	127
Kutscher . . . . .	85
Kutscher, K. H. . . . .	221. 257
Kuttner, Th. . . . .	368
Küttner . . . . .	78
Kuznitsky, E. . . . .	309
Lafay . . . . .	209
Lafay, L. . . . .	315
Lagrèze, L. . . . .	94
Laignel . . . . .	315
Lalli, G. . . . .	31
Lambelle, F. W. . . . .	366
Lambkin, F. J. . . . .	118
Lampert, P. . . . .	343
Lampé, E. . . . .	321
Lanceleur . . . . .	28
Landete . . . . .	85
Landström . . . . .	80
Lane, J. E. . . . .	224
Lange, C. . . . .	313
Langemak . . . . .	126
Langer . . . . .	52
Langes, H. . . . .	176
Langworthy . . . . .	321
Latarjet, A. . . . .	20
Latz . . . . .	273
Laubenheimer . . . . .	141
Launois . . . . .	16. 25
Lavastine . . . . .	315
Laveran . . . . .	37
Lebahn . . . . .	4
Lecerf . . . . .	321
Lederer, A. . . . .	118
Ledermann . . . . .	184
Ledermann, R. . . . .	313. 317
Lefebure . . . . .	26

	Page		Page
Lehmann, O. . . . .	233	Löwenbach, G. . . . .	13. 35
Leibkind . . . . .	296	Löwy . . . . .	193
Lemaire . . . . .	323	Lübbert . . . . .	126
Lemanski . . . . .	37	Luff, A. P. . . . .	182
Lemansky . . . . .	298	Lumpp, H. . . . .	166
Lépine, J. . . . .	70	Lundie, R. A. . . . .	114
Lereboullet . . . . .	29	Lupo . . . . .	290
Leredde . . . . .	14	Lutembacher, R. . . . .	216
Lésin, F. . . . .	185	Luxardo, A. . . . .	328
Lesser, F. . . . .	309. 316. 318		
Lessonde . . . . .	124	Macht, D. J. . . . .	301
Letulle . . . . .	19	Macleod, J. M. H. . . . .	241
Leube, v. . . . .	338	Maetzke . . . . .	301
Lévai, D. . . . .	106	Maetzke, G. . . . .	369
Levallois . . . . .	321	Malan, G. . . . .	240
Levi, E. . . . .	143	Maldarescu, N. . . . .	201. 251
Levi, L. . . . .	268	Malinowski, F. . . . .	316
Levison, Ph. . . . .	268	Mandrowski . . . . .	48. 50
Levrat . . . . .	19	Mansfeld, G. . . . .	284
Levy . . . . .	126	Marchal . . . . .	28
Levy-Bing, A. . . . .	315	Marchetti, O. . . . .	143
Lewaschew . . . . .	283	Marco Polo . . . . .	41
Lewin . . . . .	1	Marcus . . . . .	314
Lewinski . . . . .	278	Margulies, M. . . . .	313
Lewitt, M. . . . .	88. 277	Marie, P. . . . .	314. 319
Lewy, B. . . . .	363	Marks . . . . .	318
Leyden, H. . . . .	230. 318	Marshall, J. . . . .	4
Lezenius, E. . . . .	177	Martin, K. . . . .	199
Liaschenko . . . . .	200	Martin, L. . . . .	315
Lichtenberg . . . . .	146	Martinet, A. . . . .	23. 25. 209
Lill, K. . . . .	234	Martini . . . . .	127
Lindhard, J. . . . .	301	Martius, K. . . . .	318. 319
Lingen, v. . . . .	271	Marx, E. . . . .	298
Lint, v. . . . .	105	Marxer, A. . . . .	272
Lippens . . . . .	124	Massaglia . . . . .	17
Lipschütz, B. . . . .	313	Matsuoka . . . . .	124
Little, G. . . . .	147	Mattauschek . . . . .	315
Löbel . . . . .	49. 50	Matthews . . . . .	75
Loeb, H. . . . .	301	May . . . . .	47
Loeb, L. . . . .	262	Megaw, J. D. W. . . . .	183
Löer . . . . .	373	Megele . . . . .	126
Loewensohn . . . . .	49	Meidner . . . . .	311
Loewi, O. . . . .	148. 284	Meillant . . . . .	20
Loewy, A. . . . .	274	Meirowsky . . . . .	312. 313
Lohmann . . . . .	145	Meisel . . . . .	320
Lorand, A. . . . .	267	Melland, B. . . . .	75
Lorey, A. . . . .	126	Mellet, R. . . . .	357
Lotheißen . . . . .	82	Meltzer . . . . .	314



	Page
Memelsdorf . . . . .	231
Mendel 16. 20. 25. 27. 114.	141
Mendel, L. B. . . . .	145
Menudica . . . . .	321
Menuzier, G. . . . .	32
Merian, L. . . . .	347
Merkel, H. . . . .	94
Merklen, P. . . . .	19
Meszczersky, G. . . . .	108
Mettenheimer, H. v. . . . .	249
Meyer . . . . . 189. 305.	372
Meyer, E. . . . .	233
Meyer, F. . . . .	339
Meyer, G. . . . .	221
Meyer, M. . . . .	310
Meyer, R. . . . .	277
Meyerfeld, J. . . . .	295
Meyrowsky . . . . .	312
Mezernitzky . . . . .	70
Mezig . . . . .	270
Michaelis, L. . . . . 309. 313.	317
Michaelis, M. . . . .	254
Miekley . . . . .	313
Mießner . . . . . 94.	111
Milian . . . . .	314
Miller . . . . .	81
Miller, J. . . . .	262
Minet . . . . .	2
Miranda . . . . .	290
Mitchener, W. E. . . . .	248
Mitsuda . . . . .	321
Mitterer, K. . . . .	301
Modrakowski . . . . .	145
Möller, F. . . . .	370
Möllers . . . . .	56
Möllers, B. . . . .	339
Mondschein . . . . .	313
Montegazza, U. . . . .	313
Monti . . . . . 43. 53	
Moral, H. . . . .	257
Moran, J. F. . . . .	350
Morawski . . . . .	321
Morgenroth . . . . .	298
Moritz . . . . . 65.	338
Morrison, J. T. . . . .	363
Most, A. . . . .	154
Mouisset . . . . .	19
Mouneyrat . . . . .	37

	Page
Much, H. . . . .	253
Muck, O. . . . .	138
Mühsam, A. . . . .	230
Müller, A. . . . .	176
Müller, E. . . . .	236
Müller, F. . . . . 145.	338
Müller, W. . . . .	220
Müllern-Aspegren . . . . .	378
Mulzer . . . . .	117
Mulzer, P. . . . .	312
Munck, F. . . . . 314.	315
Münz . . . . .	343
Münzer . . . . .	316
Murco . . . . .	33
Murphy, J. B. . . . . 15.	314
Muskat . . . . .	248
Muto, K. . . . .	116
Nacht, A. . . . .	316
Naegeli . . . . .	108
Nagelschmidt . . . . .	313
Nagelschmidt, F. . . . .	361
Nassauer . . . . . 126.	127
Nast-Kolb . . . . .	219
Neiße, R. . . . .	187
Neiße, A. . . . . 309.	313
Nemenow . . . . .	124
Netter . . . . . 313.	315
Neu, M. . . . .	328
Neubauer, E. . . . .	346
Neugebauer, O. . . . .	108
Neumann . . . . . 278.	339
Neumayer, L. . . . .	288
Nichols, J. . . . . 311.	314
Niederstadt, B. . . . .	56
Nikitin . . . . .	321
Nitsche, F. . . . .	202
Nocht . . . . .	310
Noellner, L. . . . .	329
Noferi, U. . . . .	219
Nola, E. . . . .	165
Nomikosow, S. . . . .	109
Noorden, C. v. . . . .	321
Nordmann, O. . . . .	264
Nosek, J. . . . .	237
Notthafft, v. . . . .	227
Nouell, J. . . . .	240

	Page
Nové-Jossérand . . . . .	124
Novoa, R. . . . .	145
Ochsner . . . . .	124
Oefele . . . . .	251
Oestreich, R. . . . .	96
Oettingen, W. v. . . . .	247
Ohlemann, L. . . . .	71
Ohleyer . . . . .	242
Olchanetzki . . . . .	53
Oppenheim, H. . . . .	109
Oppenheim, W. . . . .	15. 147. 311. 314. 317
Orth . . . . .	313
Ortner, N. . . . .	338
Osborne . . . . .	321
Otto . . . . .	324
Paffrath . . . . .	372
Page . . . . .	244
Pagenstecher . . . . .	146
Pagliai, G. . . . .	264
Pagniez . . . . .	347
Pal . . . . .	362
Palm, R. . . . .	176
Panafiel, C. . . . .	329
Panfilow, P. W. . . . .	75
Pap, M. . . . .	220
Papaioannou . . . . .	220
Papinian . . . . .	219
Pascucci . . . . .	76
Pasini, A. . . . .	315. 319
Paterson, P. . . . .	243
Pätz, W. . . . .	100
Paulet . . . . .	25
Pauli . . . . .	362
Pauly . . . . .	372
Payne, E. . . . .	16
Pein, K. . . . .	323
Pellet . . . . .	321
Pépin . . . . .	319
Péraldi . . . . .	7
Pernet, G. . . . .	296
Pertik . . . . .	275
Pertik, Th. . . . .	177
Péry . . . . .	6
Peters, W. . . . .	89
Petersen . . . . .	29

	Page
Petrini . . . . .	16
Petty . . . . .	297
Peyri, J. . . . .	115
Pfab . . . . .	375
Pfeifer, J. . . . .	314
Pflughöft . . . . .	17. 107
Phoistanos, A. . . . .	313
Picard . . . . .	323
Pick . . . . .	178
Pick, E. P. . . . .	265
Pick, W. . . . .	310. 313. 314
Pieper . . . . .	65
Piericcuoli, P. . . . .	229
Pietsch, P. . . . .	284
Pikin, F. M. . . . .	79
Pineles, F. . . . .	265
Plaut . . . . .	315
Plaut, H. C. . . . .	317
Podanowski . . . . .	13
Podwyssotzki . . . . .	43. 48
Polák, B. . . . .	352
Polland, R. . . . .	181. 259. 314
Poly, F. . . . .	245
Ponomaroff . . . . .	48. 53
Pons . . . . .	346
Popow, D. . . . .	104
Porges . . . . .	215
Porges, O. . . . .	346
Porten, von der . . . . .	370
Postnikoff . . . . .	48
Pouchet . . . . .	294
Poulard . . . . .	316
Power, F. B. . . . .	328
Presas, R. . . . .	186
Preti, L. . . . .	316
Priebatsch . . . . .	208
Prinsen Geerligs . . . . .	321
Prochnow . . . . .	277
Prokhoroff . . . . .	11
Pronai, K. . . . .	97
Prunier, G. . . . .	139
Prussak . . . . .	208
Pürckhauer, R. . . . .	221
Pusey, W. A. . . . .	241
Quénu . . . . .	81
Quintana Duque, J. . . . .	319
Quisling . . . . .	159

	Page		Page
Rabena, F. . . . .	314	Rock, H. . . . .	112
Rabuteau . . . . .	4	Rodari . . . . .	275
Raices, J. A. . . . .	184	Rodolico . . . . .	275
Raimund . . . . .	347	Roger . . . . .	253
Ramacci, A. . . . .	292	Romeo, P. . . . .	281
Rapp . . . . .	313	Römer . . . . .	270
Raschkow . . . . .	202. 350	Rosenbach . . . . .	124
Ratzeburg . . . . .	335	Rosendorff, W. . . . .	370
Ravasini . . . . .	319	Rosenfeld . . . . .	347
Raven v. . . . .	110	Rosenheim, Th. . . . .	253
Raynaud . . . . .	17	Rosenthal, O. . . . .	316
Rebec . . . . .	32	Rotky, H. . . . .	138
Reber . . . . .	321	Rothschild, H. de . . . . .	268
Redlich . . . . .	315	Roques, E. . . . .	268
Regenspurger, A. . . . .	87	Rousseau, P. . . . .	197
Reich . . . . .	124	Roxirosa . . . . .	53
Reicher, K. . . . .	94	Rubow, V. . . . .	158
Reichmann, V. . . . .	314	Rückert . . . . .	324
Reid . . . . .	266	Rüdich . . . . .	67
Reinke . . . . .	319	Ruete, A. . . . .	312
Reif . . . . .	167	Ruhemann, J. . . . .	233
Reisner, V. . . . .	311	Ruhräh . . . . .	321
Rémi, S. . . . .	313	Rumpel, Th. . . . .	315. 317
Renard, J. . . . .	191		
Renault . . . . .	16	Saalfeld, E. . . . .	13. 313
Rénaut . . . . .	12. 24	Saar . . . . .	273
Renaux, E. . . . .	314	Sacchi, A. . . . .	185
Renz, W. Th. . . . .	9	Sachs . . . . .	94. 277
Renzi, E. de . . . . .	178	Såg . . . . .	150. 351
Revillet, L. . . . .	102	Sahli, H. . . . .	275
Rewidzow, O. . . . .	252	Sakubane . . . . .	331
Richter . . . . .	64	Salimbeni . . . . .	333
Richter, E. . . . .	212	Salmon, P. . . . .	313
Richter, P. . . . .	278	Salomon, O. . . . .	312
Ridlon . . . . .	124	Salway, A. H. . . . .	328
Riebold, G. . . . .	160	Salzberger . . . . .	318
Riecke . . . . .	317	Salzberger, M. . . . .	327
Riehl . . . . .	103	Sander . . . . .	277
Riehl, G. . . . .	316	Sandri . . . . .	268
Riewel, H. V. . . . .	328	Sarti . . . . .	72
Righetti, G. . . . .	329	Schade, K. . . . .	360
Rille . . . . .	317	Schaer, E. . . . .	282
Rille, H. . . . .	13	Schäfer, O. . . . .	132
Rinne . . . . .	324	Schäffer . . . . .	103
Ritter, H. . . . .	314	Schäffer, J. . . . .	299
Rivalta . . . . .	65	Schanz, A. . . . .	221
Robert . . . . .	354	Schanz, F. . . . .	315
Rocaz . . . . .	19	Schenk . . . . .	261



	Page
Schenk, F. . . . .	145
Schepelmann . . . . .	373
Scheuer, O. . . . .	88
Schick, K. . . . .	120
Schiele, W. . . . .	316. 334
Schiller . . . . .	365
Schiller, V. . . . .	81
Schindler . . . . .	231. 313. 316
Schindler, C. . . . .	119. 319. 331
Schlesinger . . . . .	315
Schlesinger, H. . . . .	167
Schlewellyn Philips . . . . .	243
Schlimpert, H. . . . .	79
Schmidt . . . . .	4
Schmidt, E. . . . .	92
Schmidt . . . . .	277
Schmidt, J. . . . .	166
Schmitt . . . . .	23
Schmitz-Pfeiffer . . . . .	79
Schnitter . . . . .	184
Schoeller, W. . . . .	83
Scholtz . . . . .	318
Scholtz, W. . . . .	218. 313
Schonnefeld . . . . .	310
Schott . . . . .	301
Schrauth, W. . . . .	83
Schreiber . . . . .	130. 309. 313
Schreiber, E. . . . .	312
Schulte . . . . .	94
Schultz-Zehden . . . . .	343
Schulz . . . . .	4
Schulze . . . . .	170. 321
Schumburg . . . . .	85
Schumm, O. . . . .	126
Schuyten . . . . .	377
Schwabe, K. . . . .	310
Schwartz, W. . . . .	311
Schwarz . . . . .	126
Schwarzwald . . . . .	347
Schweißinger, O. . . . .	239
Scipiades . . . . .	100
Seeligsohn . . . . .	316
Segelken . . . . .	220
Seidell . . . . .	266
Seiffert . . . . .	145
Selbiger . . . . .	150
Selenkowski . . . . .	169
Sellei, J. . . . .	312

	Page
Selter, H. . . . .	85
Semper, A. . . . .	234
Senator . . . . .	30
Senator, M. . . . .	149
Serano, M. . . . .	240
Serrano . . . . .	319
Siboni . . . . .	2
Sick, P. . . . .	324
Sidorenko, A. T. . . . .	206
Siebert, C. . . . .	313
Siebold, W. . . . .	202
Siegesmund, K. . . . .	337
Siegmund, A. . . . .	266
Sieskind, R. . . . .	312
Sievert, W. . . . .	208
Silberberg, L. A. . . . .	283
Silbermann . . . . .	202
Silberstein, S. . . . .	348
Silva, U. . . . .	170
Simpson, K. . . . .	133
Simrock . . . . .	316
Singer, G. . . . .	345
Sinnat, F. St. . . . .	251
Sklotowski . . . . .	39
Skonlsky . . . . .	281
Skuteki . . . . .	19
Skutetzky, A. . . . .	94
Slajmer, E. . . . .	363
Sluys . . . . .	314
Smith, W. . . . .	160
Snitowski . . . . .	319
Sobotka, P. . . . .	309. 316. 318
Sohler . . . . .	365
Solger . . . . .	67
Solowjew . . . . .	285
Soltmann . . . . .	338
Sommerfeld, P. . . . .	250
Sommerville, D. . . . .	226
Soucques . . . . .	149
Soukup, A. . . . .	152
Sourd . . . . .	347
Sowade, H. . . . .	108. 115
Sowinski . . . . .	332
Sparmberg, F. . . . .	299
Spatz, A. . . . .	292. 309
Spiegel . . . . .	343
Spiethoff, B. . . . .	310
Spiro . . . . .	235

	Page
Spitzer, E. . . . .	277. 279
Ssadowen . . . . .	41
Staby . . . . .	127
Stadlmayr . . . . .	140
Stadtfeld . . . . .	105
Stahl . . . . .	37
Stahlberg . . . . .	39
Stamm, C. . . . .	231
Stange . . . . .	39
Stanton Faust, E. . . . .	69
Stargardter, J. . . . .	183
Starkenstein, E. . . . .	181
Stauder . . . . .	126
Steimann . . . . .	124
Steinitz . . . . .	343
Stephens, G. A. . . . .	134
Stephenson, S. . . . .	281
Stepp . . . . .	248
Stern . . . . .	46
Stern, C. . . . .	313. 317
Stern, H. . . . .	268
Stevani, R. . . . .	72
Sticker, A. . . . .	136
Stift . . . . .	321
Stingl . . . . .	321
Stocker, S. . . . .	187
Stockmayer, S. . . . .	368
Stoeber, H. . . . .	322
Straub, H. . . . .	352
Strauß, A. . . . .	215. 317
Strauß, M. . . . .	154. 323
Streitberger . . . . .	219
Stricker . . . . .	171
Stringari, F. . . . .	188
Ströll . . . . .	261
Struve . . . . .	43
Studzinski, J. . . . .	192
Stuebe, R. . . . .	41
Stuelp . . . . .	312
Stumpf . . . . .	126. 128
Sturdivant Read, J. . . . .	320
Stürmer, C. v. . . . .	246
Sudeck, P. . . . .	80
Suñer, E. . . . .	182
Sylla, B. . . . .	156. 170. 281
Szerezewski . . . . .	98
Szinnyei, J. . . . .	159

	Page
Taege, K. . . . .	229. 310. 313
Tahara . . . . .	321
Talini, E. . . . .	73
Tallquist, F. W. . . . .	195
Tannhauser . . . . .	347
Tantos, J. . . . .	226
Tedesco . . . . .	319
Telemann, W. . . . .	94
Teruuchi, V. . . . .	151
Teubert, A. . . . .	111
Thalwitzer, F. . . . .	247
Thaon, P. . . . .	269
Thébault . . . . .	37
Theodoroff . . . . .	47. 48. 50
Therstappen . . . . .	318
Thilliez, M. . . . .	186
Thompson, J. A. . . . .	253
Thomson . . . . .	324
Thornton, E. N. . . . .	76
Thymowsky . . . . .	39
Tillmann . . . . .	337
Tissier . . . . .	314. 319
Tissot, R. . . . .	161
Tollens . . . . .	53. 62
Tombleson, J. B. . . . .	287
Tommasi . . . . .	35
Torday, A. v. . . . .	312
Torrance, H. . . . .	324
Touraine . . . . .	315
Touton . . . . .	187. 311. 317
Toyoda, H. . . . .	151
Traverse . . . . .	23
Tregoat, G. . . . .	173
Trembur . . . . .	127
Treupel, G. . . . .	309. 315
Tribaudeau . . . . .	314
Trimble . . . . .	321
Troisfontaines . . . . .	316
Trojanowski . . . . .	49
Troussaint . . . . .	35
Trumpf . . . . .	127
Tschugaeff . . . . .	165
Tsuru, J. . . . .	179
Tuschinsky . . . . .	318
Uebele, G. . . . .	28
Uhlenhuth, R. . . . .	117. 155. 313
Uhthoff . . . . .	312

	Page		Page
Ullmann . . . . .	315	Wegele, C. . . . .	40
Umber . . . . .	219	Weiler . . . . .	343
Unna, P. G. . . . .	146	Weiler, F. . . . .	318
Underhill, F. P. . . . .	148	Weinfurter . . . . .	319
Ungar, K. . . . .	336	Weintraud . . . . .	311. 313
Unger . . . . .	219	Weiß . . . . .	43. 48
Unna, P. G. . . . .	318. 366. 376	Weiß, A. . . . .	303
Ussher, C. D. . . . .	135	Weiß, M. . . . .	289
Utz . . . . .	189	Welander . . . . .	5
		Welander, E. . . . .	115
Vajas . . . . .	37. 43	Wendt, E. . . . .	370
Valentini . . . . .	293	Werner . . . . .	146. 282. 379
Variot . . . . .	19. 37	Werner, H. . . . .	310. 311
Vassmer . . . . .	191	Werner, R. . . . .	155
Veiel, E. . . . .	160	Werther . . . . .	316
Veit, R. . . . .	360	Wertheimer-Raffalovich, R. . . . .	274
Velden, v. d. . . . .	190	Wesenberg, G. . . . .	231
Veress, Fr. v. . . . .	112	Wessely, K. . . . .	322
Verotti, G. . . . .	13	Wettstein, E. . . . .	221
Verth . . . . .	137	White, J. A. H. . . . .	269
Vetlesen, H. J. . . . .	195	Wibo . . . . .	317
Viannay . . . . .	220	Wickham, L. . . . .	14
Vidakowich . . . . .	124	Widal, F. . . . .	19
Vigenaud . . . . .	37	Wilke . . . . .	50
Villanova, P. . . . .	115	Williams . . . . .	321
Vogel, O. E. . . . .	374	Williams, L. . . . .	182. 269
Vogelmann, R. . . . .	79	Willige, H. . . . .	25. 315
Vogt . . . . .	265	Windaus, A. . . . .	162
Volhard, F. . . . .	207	Windrath . . . . .	126
Volk, R. . . . .	311. 313	Winqvist, G. . . . .	285
Volte, R. . . . .	315	Wittgenstein . . . . .	271
Voronoff, G. . . . .	316	Witthauer, K. . . . .	230
		Wolff . . . . .	310
Waelsch, L. . . . .	199	Wölffer . . . . .	374
Wälsch . . . . .	315	Wolfram . . . . .	372
Wagner . . . . .	356	Wolters . . . . .	184
Wagner, G. A. . . . .	365	Wray, G. G. . . . .	269
Wagner, K. E. . . . .	267	Wright . . . . .	133
Wallace, A. J. . . . .	83	Wucher . . . . .	226
Walter . . . . .	350	Wyss, H. v. . . . .	252
Walter, E. . . . .	121	Wyss, M. O. . . . .	154
Walterhöfer . . . . .	183		
Walther . . . . .	126	Yakimoff . . . . .	319
Ward, S. B. . . . .	255	Yasuki . . . . .	331
Watraszewski, X. v. . . . .	313	Yoshimura . . . . .	321
Waugh, W. F. . . . .	120. 353		
Weber, H. . . . .	153. 318	Zarubin . . . . .	318
Wechselmann, W. . . . .	309. 313. 315. 316	Zatti, C. . . . .	123



	Page		Page
Zeißl, M. v. . . . .	312. 313	Zoltan . . . . .	362
Zelenew . . . . .	319	Zuelzer . . . . .	271. 272
Zeller, A. . . . .	155	Zumbusch, L. v. . . . .	259
Zickgraf . . . . .	239	Zupitza . . . . .	110
Zieler, K. . . . .	314. 315	Zweifel . . . . .	68. 100
Zielinsky, W. . . . .	279	Zweifel, P. . . . .	127
Zilz, J. . . . .	191. 279	Zweig . . . . .	241
Zirm, E. . . . .	168		

---

# General Index.

	Page		Page
Acetone . . . . .	65	Arrhenal . . . . .	37
Acidum aceticum . . . . .	65	Arsacetin . . . . .	107
» boricum . . . . .	66	Arsenobenzol = Salvarsan . . . . .	304
» cacodylicum . . . . .	2	Arsenophenylglycin . . . . .	110
» hydrochloricum . . . . .	67	Arsentriferrin . . . . .	111
» lacticum . . . . .	68	Arsinal . . . . .	37
» nucleinicum . . . . .	69	Arthigon . . . . .	331
» picricum . . . . .	71	Asurol . . . . .	112
» sulphurosum . . . . .	73	Atoxyl . . . . .	114
Adalin . . . . .	73	Atoxylic mercury . . . . .	117
Adrenalin . . . . .	75	Atropine . . . . .	118
Adrenochrom . . . . .	77		
Æther . . . . .	78	Benzidine . . . . .	120
Æthyl chloridum . . . . .	81	Benzin Petrolei . . . . .	123
Æthyleni chloridum . . . . .	82	Bismuthi carbonas . . . . .	126
Afridol . . . . .	83	» subnitras . . . . .	123
Alcohol . . . . .	84	Black ointment . . . . .	103
» amylicum . . . . .	86	Bolus alba sterilisata . . . . .	126
Allophanic ester of Santalol . . . . .	87	Bornyval . . . . .	129
Allosan . . . . .	87	Bromalin . . . . .	129
Alsol . . . . .	88	Bromdiethylacetyl urea . . . . .	73
Aluminii aceto-tartras . . . . .	88	Bromipin . . . . .	130
Alypin . . . . .	89	Bromural . . . . .	131
Amido-azotoluol . . . . .	91	Brovalol . . . . .	368
Ammonii molybdis . . . . .	92		
Ammonium thiocyanate . . . . .	363	Cacodylates . . . . .	1
Anthrasol . . . . .	92	Cacodylic acid . . . . .	2
Anthrax Serum . . . . .	331	» » preparations . . . . .	1
Antiformin . . . . .	93	Cacodylic cinnamic acid . . . . .	33
Antipyrin . . . . .	95	Calcii chloridum . . . . .	133
Antithyroidin-Moebius . . . . .	329	» lactas . . . . .	133
Antituman . . . . .	96	» permanganas . . . . .	134
Aperitol . . . . .	97	» sulphas . . . . .	135
Apomorphin. hydrochl. . . . .	99	Camphora . . . . .	135
Arecolin . . . . .	100	Carbenzyme . . . . .	136
Argenti acetas . . . . .	100	Carbo animalis . . . . .	138
» nitras . . . . .	101	Carbonic acid . . . . .	240
Argentum colloidal . . . . .	103	» » snow . . . . .	240
Argyrol . . . . .	105	Chinolin. sulphosalicyl. . . . .	139
Aristochin . . . . .	106	Chlorethyl . . . . .	81

	Page		Page
Chloral Hydrate . . . . .	139	Faex medicinalis . . . . .	179
Chlor-meta-cresol . . . . .	141	Ferri cacodylas . . . . .	2. 29
Chloroform . . . . .	142	Fibrolysin . . . . .	181
Cholera Serum . . . . .	333	Filmaron . . . . .	188
Cholesterin . . . . .	144	Fluoresceïn . . . . .	189
Cholin . . . . .	145	Folia Digitalis . . . . .	157
Chromium water . . . . .	286		
Chrysarobin . . . . .	146	Gelatina sterilisata . . . . .	190
Chrysophanic yellow . . . . .	367	Glandulae Parathyroideae . . . . .	263
Cocaine . . . . .	148	» Salivales . . . . .	264
Collargol . . . . .	103	» Thymi . . . . .	264
Corpora lutea . . . . .	262	» Thyroideae . . . . .	265
Coryfin . . . . .	150	Globularin . . . . .	193
Cuorin . . . . .	151	Glucose . . . . .	194
Cupferron . . . . .	152	Glycerin . . . . .	195
Cycloform . . . . .	153	Gomenol . . . . .	196
		Gonococcic Serum . . . . .	334
Diamido-anthraquinone sulphonic		» vaccine . . . . .	331
acid . . . . .	155	Gonosan . . . . .	188
Diaspirin . . . . .	156	Grape Sugar . . . . .	194
Dichlorethane . . . . .	82	Guaiacol . . . . .	199
Digipuratum . . . . .	159	» arsenic . . . . .	201
Digitalis Substances . . . . .	157	» cacodylate . . . . .	3
Digitonin . . . . .	162	» carbonate . . . . .	199
Digitoxin . . . . .	163	Guaiacose . . . . .	199
Dimethylglyoxim . . . . .	165	Gynoval . . . . .	202
Di-9, 10 monoxyphenanthryl-			
amine . . . . .	166	Hectargyre . . . . .	204
Dionin . . . . .	167	Hedonal . . . . .	205
Dioxidiamido-arsenobenzol . . . . .	304	Hectin . . . . .	203
Diplosal . . . . .	170	Hegonon . . . . .	207
Diuretin . . . . .	171	Hirudin . . . . .	207
		Hordenin. sulphas . . . . .	209
Ehrlich-Hata-Preparation "606" . . . . .	304	Hormonal . . . . .	272
Endo-agar . . . . .	299	Hydrargyri benzoas . . . . .	209
Endo Tablets . . . . .	299	» biniodidum . . . . .	210
Endotin . . . . .	338	» iodidum . . . . .	211
Enesol . . . . .	172	» iodo-cacodylas . . . . .	34
Epithermol gauze . . . . .	91	» cacodylas . . . . .	3. 33
Ethyl chloride . . . . .	81	» metallicum . . . . .	212
Ethylene chloride . . . . .	82	» nitras . . . . .	213
» dichloride . . . . .	82	» oxycyanidum . . . . .	214
Eucalyptol . . . . .	174	» salicylas . . . . .	215
Eugallol . . . . .	175	Hydropyrin . . . . .	216
Eumenol . . . . .	176	Hypophysin . . . . .	269
Eumydrin . . . . .	177	Hypophysis cerebri . . . . .	268
Europhen . . . . .	178		
Extractum filicis liquidum . . . . .	178	Ichthyol . . . . .	216
		Indian Ink (Burri) . . . . .	218



	Page
Iodarsyl . . . . .	114
Iodine . . . . .	219
Iodine-ethylene chloride solution . . . . .	83
Iodoglidine . . . . .	227
Iodo-glycerin . . . . .	222
Iodo-gomenol . . . . .	197
Iodo-guaiacol . . . . .	201
Iodipin . . . . .	222
» pro usu veterinario . . . . .	224
Iodival . . . . .	226
Iodomenin . . . . .	228
Iothion . . . . .	229
Isoform . . . . .	231
Iron Sajodin . . . . .	232
Kaolin, sterilised . . . . .	126
Kamala . . . . .	234
Kephaldol . . . . .	234
Kephir . . . . .	39
Lactolavol . . . . .	68
Lenicet . . . . .	235
Lentocalin . . . . .	270
Leucofermantin . . . . .	236
Lien . . . . .	270
Limonen . . . . .	239
Liquor Calcis . . . . .	241
Lithii acetylosalicylas . . . . .	216
» cacodylas . . . . .	3
Lysochlor . . . . .	142
Magnesii cacodylas . . . . .	35
» carbonas . . . . .	242
» chloridum . . . . .	242
» sulphas . . . . .	243
Magnesium-Perhydrol . . . . .	245
Mangani cacodylas . . . . .	3
Mastix . . . . .	247
Medulla ossium . . . . .	270
Meningococcic Serum . . . . .	334
Menthol . . . . .	248
Mergal . . . . .	249
Methyl di-sodium arsenate . . . . .	37
Methylene blue . . . . .	250
Milk poor in sugar . . . . .	379
Monochlorphenol . . . . .	276
» camphor . . . . .	276

	Page
Naphthol- $\alpha$ - . . . . .	251
Nastin . . . . .	252
Neurin . . . . .	253
Neutralon . . . . .	253
Niaouli oil . . . . .	196
Nile red . . . . .	366
Nitroglycerin . . . . .	254
Novaspirin . . . . .	255
Novocaine . . . . .	256
Novoiodin . . . . .	258
Oleum Chenopodii anthelminthici . . . . .	259
» Niaouli . . . . .	196
» Terebinthinae . . . . .	260
Olintal . . . . .	261
Orcin . . . . .	261
Organo-therapeutic preparations . . . . .	262
Ovaria . . . . .	271
Ovogal . . . . .	273
Pancreas-Hormone . . . . .	271
Pantopon . . . . .	274
Parathyroidin . . . . .	263
Pergenol . . . . .	277
Perhydrol . . . . .	278
Periplocin . . . . .	283
Peristaltic-Hormone . . . . .	272
Peristaltin . . . . .	284
Physostigmine . . . . .	284
Picric acid . . . . .	71
Pituitrin . . . . .	269
Potassii bichromas . . . . .	286
» cacodylas . . . . .	2
» permanganas . . . . .	234
» tartras acidus . . . . .	289
Protargol . . . . .	290
Pyocyanase . . . . .	292
Pyramidon . . . . .	293
Pyrogallol dimethyl ether . . . . .	295
Quinine . . . . .	296
» cacodylate . . . . .	2
» bisulphate . . . . .	297
» hydrobromide . . . . .	298
» hydrochloride . . . . .	296
» hydrochloro-carbamide . . . . .	297
» tannate . . . . .	297

	Page
Ragit . . . . .	298
Ragit-Agar . . . . .	299
» broth . . . . .	299
Resorcin . . . . .	299
Rongalite white . . . . .	367
Sabromin . . . . .	300
Saccharose . . . . .	209
Safranin . . . . .	301
Sajodin . . . . .	303
Salivary gland . . . . .	264
Salol . . . . .	303
Salvarsan . . . . .	304
Santyl . . . . .	320
Sarton . . . . .	320
Scarlet red . . . . .	322
Scopolamine . . . . .	324
Semen Cucurbitae Pepo . . . . .	328
Sera and Antigens . . . . .	329
Silver nitrate ammoniacal albumoses . . . . .	207
Sodii cacodylas . . . . .	2. 11. 343
» choleinas . . . . .	345
» chondroitin sulphas . . . . .	96. 346
» glycocholas . . . . .	346
» iodidum . . . . .	347
» monomethyl arsenas . . . . .	36
» nucleinas . . . . .	69
» perboras . . . . .	348
» peroxidum . . . . .	348
» thiocyan. . . . .	362
Soja bean . . . . .	320
Sophol . . . . .	349
Spirosal . . . . .	350
Streptococcic Serum . . . . .	335
Strophanthin . . . . .	351
Strychnine . . . . .	352
» arsenate . . . . .	353
» cacodylate . . . . .	4. 36
Stypticin . . . . .	353
Substitol . . . . .	354
Sulphoform . . . . .	358

	Page
Sulpho-naphtholazo-m-oxybenzoic acid . . . . .	357
Suptol Burow . . . . .	337
Syphilis reagent of v. Dungern . . . . .	340
Taka-Diastase . . . . .	359
Tanargentan . . . . .	360
Tannyl . . . . .	360
Thallii carbonas . . . . .	361
Thilaven . . . . .	361
Thiocyanates . . . . .	362
Thiozone . . . . .	361
Thyroidin . . . . .	265
Tinctura Pyrethri rosei . . . . .	362
Triphenyl antimonyl sulphide . . . . .	358
Tropacocaine . . . . .	363
Trypsin . . . . .	365
Tuberculin . . . . .	337
Tuberculol . . . . .	337
Typhoid Serum . . . . .	339
Unguentum Hydrarg. iodidi pultiforme . . . . .	211
Unna's Skin Reagents . . . . .	366
Urotropine . . . . .	367
Valisan . . . . .	368
Veratrine . . . . .	369
Veronal . . . . .	369
» -Sodium . . . . .	369
Wassermann's Syphilis Test . . . . .	340
Xerax capsules . . . . .	180
» powder . . . . .	180
Yohimbine . . . . .	373
Zinci acetas . . . . .	375
» sulphas . . . . .	376
Zinc eucrine gelanth . . . . .	376
Zincopyrin . . . . .	377
Zinc-Perhydrol . . . . .	378

# Index of Diseases, Symptoms and Indications for Treatment.

	Page		Page
Abortion (Atropine) 120; (Corpora lutea) . . . . .	263	Anaphrodisia vet. (Yohimbine)	373
Abscesses (Calcium sulphide) 135; (Gomenol) 196; Potass. permangan.) 287; (Leucofermantin) 237; (Novoiodin) 258; (Resorcin) 300; (Trypsin) . . . . .	365	Angina pectoris (Bromural) 132; (Digitalis) 158; (Magnes. Perhydrol) 245; (Nitroglycerin) . . . . .	254
Achylia (Taka-Diastase) . . . . .	360	» pectoris spuria (Magnes. Perhydrol) . . . . .	245
Acne (Alumin. acet.) 89; (Fæx medic.) 181; (Sod. cacodyl.) 10	10	Angioma cavernosum (Potass. permangan.) . . . . .	288
Actinomycosis (Iodipin) . . . . .	226	Anguillulosis (Glycerin) . . . . .	196
Adenitis (Sod. cacodyl.) . . . . .	10	Ankylostomiasis (Gomenol) . . . . .	197
Adhesions (Fibrolysin) . . . . .	182	Anthrax (Serum) 331; (Bitartrate of potassium) . . . . .	290
Adiposity (Gland. Thyroid.) . . . . .	268	Aortitis chron. (Fibrolysin) . . . . .	186
Agoraphobia (Bornyval) . . . . .	129	Apoplexy (Iodival) . . . . .	227
Alcoholism (Scopolamine) . . . . .	328	Appendectomy (Leucofermantin) . . . . .	238
Alopecia, seborrhœic (Sulphoform) . . . . .	358	Arterio-sclerosis (Bromural) 132; (Digipuratum) 161; (Diuretin) 171; (Gynoval) 203; (Iodival) 227; (Iodomenin) 228; (Sajodin) 303; (Stypticin) . . . . .	354
Amenorrhœa (Eumenol) . . . . .	176	Arthritis chron. (Fibrolysin) . . . . .	181
Anæmia (Sod. cacodyl.) 10; 23; 344; (Ferri cacodyl.) 30; (Kephir) 52; (Cholesterin) 144; (Digipuratum) 161; (Iron Sajodin) . . . . .	232	» deformans (Fibrolysin) 181; (Hydropyrene) . . . . .	216
» perniciosa (Ferri cacodyl.) 31; (Kephir) 52; (Acid. hydrochlor.) 67; (Glycerin) 195; (Sod. cacodyl.) . . . . .	344	» gonorrhœica (Resorcin) . . . . .	300
» splenica (Sod. cacodyl.) . . . . .	344	» metastatica (Iodipin) . . . . .	225
Anæsthesia (Ether) 78; (Ethyl chloride) 82; (Chloralhydrate) 139; (Chloroform) 142; (Hedonal) 205; (Pantopon) 274; (Scopolamine) 324; (Tropacocaine) . . . . .	363	Articular rheumatism (see Rheumatism, articular).	
Anal fissures (Aperitol) 99; (Cycloform) . . . . .	155	» rigidity (Fibrolysin) . . . . .	182
Anaphrodisia (Bornyval) . . . . .	129	» tuberculosus (Carbenzyme) . . . . .	137
		Ascaridiasis (Oleum Chenopod.) . . . . .	259
		Ascites (Acidum nucleic.) 70; (Adrenalin) 76; (Digipuratum) . . . . .	161
		Asthma (Sod. cacodyl.) 23; (Sod. monomethylarsen.) 37; (Adrenalin) 75; (Eumydrin) 177; (Iodival) 227; (Gland. Thyroidea) . . . . .	268



	Page
Asthma bronchiale (Sajodin) . . . . .	303
Asystolia (Strophanthin) . . . . .	351
Auditory meatus, furunculosis (Spirosal) . . . . .	351
Balanitis gangrenosa (Perhydrol) . . . . .	281
Bedsore (Cycloform) 155; (Pot. permangan.) . . . . .	288
Blackwater fever (Cholesterin) . . . . .	144
Bladder tuberculosis (Collargol) . . . . .	104
Bleaching, Method of (Sod. perboras.) . . . . .	348
Blepharitis (Sod. cacodyl.) 27; (Collargol) 104; (Hydrarg. biniod.) 211; (Perhydrol) . . . . .	349
Blepharo-conjunctivitis (Collargol) . . . . .	104
Blepharospasm (Hydrarg. biniod.) . . . . .	211
Blood detection (Benzidine) . . . . .	120
Bone tuberculosis (Carbenzyme) . . . . .	137
Bothricephalus anæmia (Glycerin) . . . . .	195
Bright's disease (Kephir) . . . . .	52
Bronchial catarrh (Kephir) . . . . .	52
Bronchiolitis (Digipuratum) . . . . .	161
Bronchitis (Sod. cacodyl.) 23; (Digipuratum) 161; (Iron Sajodin) 233; (Eucalyptol) 174; (Gomenol) 196; (Iodival) . . . . .	227
» bronchiectasis (Limonene) . . . . .	239
» fœtida (Limonene) . . . . .	239
Bronchopneumonia (Collargol) 105; (Digitoxin) . . . . .	163
Burns (Argent. nitras.) 102; (Cycloform) 155; (Magnes. carbonas.) 242; (Alsol) . . . . .	89
Cachexia (Sod. cacodyl.) 11; (Kephir) 52; (Gland. salivales) . . . . .	264
Cancroids (Pot. permangan.) . . . . .	288
Carbuncles (Alcohol) 84; (Pot. permangan.) . . . . .	288
Carcinoma (Sod. cacodyl.) 16; (Alcohol. amylic.) 86; (Antituman) 97; (Kaolin) 127; (Substitol) 354; (Trypsin) . . . . .	366
Cardialgia (Gynoval) . . . . .	203

	Page
Cataracta senilis (Sod. iodid.) . . . . .	348
» traumatica (Europhen) 178; (Sod. iodid.) . . . . .	348
Cellulitis (Alcohol) 84; (Pot. permangan.) 287; (Novo-iodin) . . . . .	258
» vet. (Fibrolysin) 188; (Iothion) 231; (Zinc-Perhydrol) . . . . .	379
Cephalalgia (Hydropyrine) . . . . .	216
Cervix, catarrh of the (Fæx medic.) . . . . .	180
Chest, inflammation of the (vet.) (Atoxyl) . . . . .	116
Chloro-anæmia (Ferri cacodyl.) . . . . .	30
Chlorosis (Sod. cacodyl.) 23; (Ferri cacodyl.) 30; (Kephir) 52; (Arsentriferrin) 111; (Bromural) 132; (Digipuratum) 161; (Iron Sajodin) . . . . .	232
Cholelithiasis (Ovogal) . . . . .	274
Cholera (Kaolin) 129; (Serum) 333; (Glucose) 195; (Veratrine) . . . . .	369
» nostras (Veratrine) . . . . .	369
Chorea (Sod. cacodyl.) 25; 344; (Sod. monomethylarsen.) 37; (Kephir) 52; (Sabromin) . . . . .	301
Climacteric disturbances (Valisan) . . . . .	368
Colitis (Aperitol) 99; (Magnes. chlorid.) . . . . .	243
Colon catarrh (Gelatina) 192; (Protargol) . . . . .	292
Colpitis (Fæx medic.) . . . . .	180
Coma diabeticum (Magnesium-Perhydrol) . . . . .	246
Conjunctival catarrh . . . . .	72
» inflammation, vet. (Zinc Perhydrol) . . . . .	379
» injuries (Acid. picric.) . . . . .	71
» tuberculosis (Acid. lactic.) . . . . .	69
Conjunctivitis (Argyrol) . . . . .	106
» Meibomiana (Perhydrol) . . . . .	281
Contusions (Substitol) . . . . .	356
Constipation (Kephir) 52; (Aperitol) 98; (Magnes. chlorid.) 242; (Sod. cholein.) 345; (Hormonal) . . . . .	272

	Page
Convalescence (Kephir) . . .	52
Coprostasis (Magnes. chlorid.)	243
Corneal burns (Acid. picric.)	71
» injuries (Zinc-Perhydrol)	
379; (Acid. picric.) . . .	71
» opacity (Dionin) . . .	168
» phlyctenules (Hydrargyr.	
biniod.) . . .	211
» scars (Dionin) . . .	168
» ulcer (Sod. cacodyl.) 27;	
(Argyrol) 106; (Perhydrol)	281
» vet. (Fibrolysin) . . .	188
Coxalgia (Sod. cacodyl.) . . .	18
Coxitis (Bismuth subnitr.) 124;	
(Fibrolysin) . . .	181
Cretinism (Gland. Thyroid.) . .	267
Cysticercus (Extract. Filicis) . .	178
Cystitis (Allosan) 88; (Collar-	
gol) 104; (Gonosan) . . .	198
Dacryocystitis (Collargol) . . .	104
Dawning Sleep (Scopolamine)	326
Delirium (Acid. nuclein.) . . .	70
» tremens (Veronal) . . .	371
Dementia præcox (Acid. nuclein.)	
70; (Gland. Thyroid.) . . .	268
Dermatitis (Aluminium acetic.	
tartar.) . . .	89
» exfoliativa (Quinine) . . .	296
» herpetiformis (Sod. caco-	
dylic.) . . .	10
Dermatoses (Hydrarg. iodo-caco-	
dylic.) 35; (Eugallol) . . .	175
Diabetes (Sod. cacodylic.) 12;	
(Magnes. Perhydrol) 246;	
(Sarton) 320; (Milk poor	
in sugar) . . .	379
» insipidus (Arsacetin) 110;	
(Globularin) . . .	193
» mellitus (Sod. cacodyl.) 27;	
(Kephir) 52; (Globularin)	193
Diarrhœa (Novaspirin) 255;	
(Pantopon) . . .	275
» chron., vet. (Tanargentan)	360
Diphtheria (Digipuratum) 161;	
(Olontal) . . .	261
Disinfection (Antiformin) . . .	93
Distemper diarrhœa (Tannyl) . .	361

	Page
Dupuytren's Contraction (Fibro-	
lysin) . . .	184
Dysentery (Kephir) 52; (Aper-	
itol) 99; (Argent. nitras) 102;	
(Hordenin) . . .	209
Dysmenorrhœa (Iron Sajodin)	
233; (Eumenol) 176; (Hydro-	
pyrine) . . .	216
Dyspepsia (Magnes. chlorid.) . .	243
Ears, buzzing in the (Bromural)	132
Eclampsia gravidarum (Hirudin)	207
Ecthyma (Ichthyol) . . .	217
Eczema (Alumin. acet. tartar.)	
89; (Kaolin) 128; (Cycloform)	
155; (Iothion) 230; (Sod.	
cacodyl.) 344; (Scarlet Red)	
323; (Sulphoform) . . .	359
Emphysema (Sod. monomethyl-	
arsen.) 37; (Stypticin) . . .	354
Empyema (Naphthol) . . .	251
» of the antrum of Highmore	
(Perhydrol) . . .	279
Endocarditis (Diplosal) . . .	170
Endometritis (Fibrolysin) 185;	
(Novoidin) . . .	258
Enteritis (Kaolin) 128; (Cho-	
lesterin) 144; (Guaiacol	
200; (Magnes. chlorid.) . .	243
» mucomembranacea (Hor-	
denin) . . .	209
Enuresis (Gland. Thyroid.) . . .	268
Epididymitis (Alcohol) 84; (Al-	
losan) 87; (Resorcin) . . .	300
Epilepsy (Adalin) 74; (Bromi-	
pin) 131; (Gynoval) 203; (Sab-	
romin) . . .	301
Episcleritis (Dionin) . . .	169
Epistaxis (Atropine) . . .	120
Epithelial thickening (Eugallol)	175
Epithelioma (Carbonic acid.) . .	240
Erosions (Dionin) . . .	168
Erysipelas (Alcohol) 84; (Digi-	
puratum) . . .	161
Erythema exsudativum (Alsol) . .	89
Excitement (Veronal) . . .	371
Eye, affections of the (Sod.	
cacodyl.) 27; (Acid. boric.) 66;	

	Page
(Acid. picric.) 71; (Diaspirin) 156; (Dionin) 168; (Hydrarg. biniod.) 210; (Sod. iodid.) 348; (Perhydrol) . . . . .	281
Fear (Gynoval) 202; (Magnes. Perhydrol) . . . . .	245
Fibrositis (Fibrolysin) . . . . .	182
Fistulæ (Bismuth. subnitr.) 123; (Potass. permangan.) 288; (Leucofermantin) 238; (Pergenol) . . . . .	277
» vet. (Perhydrol) . . . . .	282
Flatulence (Veronal) . . . . .	372
Fluor albus (Iothion) . . . . .	230
Foal, lameness in (Iodipin) . . . . .	225
Folliculitis (Coryfin) 151; (Ichthyol 217; (Spirosal) . . . . .	351
Frambæsia (Salvarsan) . . . . .	308
Fungus (Pot. permangan.) . . . . .	288
Furuncles (Alsol) 89; (Argent. nitr.) 102; (Ichthyol) 217; (Pot. permangan.) 287; (Pergenol) 278; (Resorcin) . . . . .	300
Furunculosis (Coryfin) 151; (Fæx med.) . . . . .	181
Galls, vet. (Iothion) . . . . .	231
Gall stones (Kephir) . . . . .	52
Gastric cancer (Sod. cacodyl.) . . . . .	12
» carcinoma (Antituman) . . . . .	96
» diseases (Kephir) 50; (Protargol) 292; (Glucose) . . . . .	195
» neuroses (Valisan) . . . . .	369
» ulcer (Salol) . . . . .	303
Gastro-enteritis (Calcium permangan.) 134; (Protargol) 292	
» intestinal catarrh (Carbenzyme) 138; (Tannyl) 361; (Glucose) . . . . .	195
Giddiness (Bromural) 132; (Gynoval) . . . . .	203
Gingivitis (Iothion) . . . . .	231
Glands, inflamed (Alcohol) . . . . .	84
» swollen (Arsacetin) 108; (Arsentriferrin) 112; (Iothion) . . . . .	231

	Page
Glaucoma (Dionin) . . . . .	169
Gonorrhœa (Allosan) 87; (Alsol) 89; (Atropine) 119; (Gonosan) 198; (Hegonon) 207; (Isoform) 231; (Perhydrol) 281; (Protargol) 290; (Pyocyanase) 292; (Santyl) 320; (Arthigon) 331; (Serum) . . . . .	334
» posterior (Allosan) . . . . .	88
Gonorrhœal rheumatism (Spirosal) . . . . .	350
Gout, (Acid. hydrochlor.) 67; (Adrenochrom) . . . . .	77
Granulations (Carbonic acid.) . . . . .	241
Granuloma (Pot. permangan.) . . . . .	288
Graves's Disease (Sod. cacodyl.) 12; 26; (Atoxyl) 114; (Hypophysis) 269; (Antithyroidin) . . . . .	329
Hæmophilia (Atropine) 120; (Calc. lact.) 133; (Lien) . . . . .	278
Hæmoptysis (Atropine) 120; (Quinine) . . . . .	297
Hæmorrhage (Atropine) 120; (Calc. lact.) 133; (Gelatina steril.) 192; (Stypticin) . . . . .	353
Hæmorrhoids (Aperitol) . . . . .	99
Hair, diseases of the (Afridol) . . . . .	84
Hand, eczema (Anthrasol) . . . . .	93
Hay fever (Cocaine) 149; (Coryfin) . . . . .	151
» fever conjunctivitis (Cocaine) . . . . .	149
Headache (Bromural) 132; (Coryfin) 150; (Gynoval) 203; (Kephaldol) 235; (Pyramidon) 294	
Heart disease (Digitalis) 157; (Digipuratum) 159; (Digitoxin) 163; (Fibrolysin) 186; (Gynoval) 203; (Periplocin) 283; (Strophanthin) 351; (Stypticin) . . . . .	354
» , fatty (Iron Sajodin) 233; (Sajodin) . . . . .	303
» insufficiency (Digitalis) 158; (Digipuratum) . . . . .	159
» neuroses (Bromural) . . . . .	132



	Page
Heart, palpitation of the (Bromural) 132; (Gynoval) . . . . .	203
Heat, chronic (vet.) Arsenophenylglycin . . . . .	111
Hepatitis interstitialis (Fibrolysin) . . . . .	184
Herpes iris (Sod. cacodyl.) . . . . .	13
» zoster (Alcohol) . . . . .	84
Hydrothorax (Digipuratum) . . . . .	160
Hygroma (Trypsin) . . . . .	366
Hyperacidity (Neutralon) 254; (Novaspirin) . . . . .	255
Hyperchlorhydria (Magnesium-Perhydrol) 245; (Taka-Diastase) . . . . .	360
Hyperemesis gravidarum (Sod. monomethylarsen.) 37; (Gland. Thyroid.) 266; (Glucose) 195; (Valisan) . . . . .	369
Hyperidrosis (Alsol) . . . . .	89
Hypersecretion (Neutralon) . . . . .	254
Hyperthermia (Quinine) 298; (Pyramidon) . . . . .	295
Hypopion (Europhen) . . . . .	178
Hysteria (Kephir) 52; (Arsentriferrin) 111; (Bromural) 132; (Gynoval) 203; (Novaspirin) 255; (Valisan) . . . . .	368
Hysterical muscular weakness (Sod. cacodyl.) . . . . .	25
Ileus (Atropine) . . . . .	118
Impetigo contagiosa (Alsol) 89; (Sulphoform) . . . . .	359
» simplex (Sulphoform) . . . . .	359
Incompensation (Digipuratum) . . . . .	160
Incontinentia urinæ (Bornyval) 129	
Influenza (Digipuratum) 161; (Novaspirin) . . . . .	255
Inguinal gland inflammation (Resorcin) . . . . .	300
Inguinal hernia (Scopolamine) . . . . .	328
Insanity (Sod. cacodyl.) 25; (Adalin) . . . . .	74
Insomnia (Adalin) 74; (Bornyval) 129; (Bromipin) 131; (Bromural) 132; (Gynoval) 203; (Veronal & Veronal-Sodium) 370	

	Page
Intercostal neuralgia (Gynoval) 203; (Hydropyrine) . . . . .	216
Intermittent fever (Sod. monomethylarsen.) . . . . .	37
Intertrigo (Alumin. acet. tartar.) 89; (Kaolin) 128; (Cycloform) 155; (Zinc eucrine gelanth.) 376	
Intestinal catarrh (Kephir) . . . . .	52
» diseases (Kephir) 49; (Kaolin) 127; (Hordenin) 209; (Magnes. chlorid.) 243; (Novaspirin) . . . . .	255
» paralysis (Hormonal) . . . . .	273
» paresis (Sod. cholein.) 345; (Physostigmine) . . . . .	285
Iridectomy (Dionin) . . . . .	169
Iridocyclitis (Dionin) . . . . .	169
Iritis (Dionin) 169; (Europhen) 178	
Joints, inflammation of the (Alcohol) . . . . .	84
Keloid (Potass. permangan.) . . . . .	288
Keratitis (Argyrol) . . . . .	106
» bullosa (Sod. cacodyl.) . . . . .	27
» neuroparalytica (Dionin) . . . . .	169
» parenchymatosa (Dionin) . . . . .	168
Kidney diseases (Kephir) . . . . .	52
» , hæmorrhage of the (Atropine) . . . . .	120
» , tuberculosis of the (Bismuth. subnitr.) . . . . .	124
Labour pains (Pantopon) 275; (Veronal) . . . . .	372
Lachrymal sac, suppuration of (Perhydrol) . . . . .	281
Laparotomy (Carbenzime) . . . . .	137
Laryngitis (Iron Sajodin) . . . . .	233
Lead poisoning (Calc. permangan.) . . . . .	135
Leg, ulcers of the (Argent. nitric.) . . . . .	103
Leprosy (Sod. cacodyl.) 17; (Guaiacol) 201; (Nastin) 253; (Salvarsan) . . . . .	308
Leukæmia (Sod. cacodyl.) 12; 23; (Ferri cacodyl.) . . . . .	30

	Page
Lichen ruber planus (Sod. cacodyl.) 10; 13; 344; (Arsacetin) 110; (Salvarsan) . . . . .	308
Lipoma (Potass. permangan.) . . . . .	288
Liver affections (Magnes. chlor.) 243; (Stypticin) . . . . .	354
» , catarrh of the (Ovocal) . . . . .	274
» , cirrhosis of the (Acid. nuclein.) 70; (Pot. bitart.) . . . . .	289
Local anæsthesia (Alypin) 89; (Quinine) 296; (Cocaine) 149; (Dionin) 169; (Carbonic acid.) 240; (Novocain) . . . . .	257
Lumbago (Diplosal) . . . . .	170
Lumbar anæsthesia (Tropococaine) . . . . .	363
Lung gangrene (Eucalyptol) 174; (Limonene) . . . . .	239
» œdema (Nitroglycerin) . . . . .	251
» tuberculosis (Acid. cacodylic.) 8; (Sod. cacodylic.) 10; 20; (Guaiacol cacodylic.) 32; (Kephir) 39; (Acid. sulphur.) 73; (Col-largol) 105; (Atoxyl) 115; (Eucalyptol) 174; (Guaiacol) 199; Pot. bichrom.) . . . . .	286
Lupus (Iodo-guaiacol) 202; Pot. permangan.) . . . . .	288
» erythematodes (Sod. cacodyl.) 10; (Carbonic acid.) . . . . .	240
Lymphadenitis (Ferri cacodyl.) 30; (Alcohol) . . . . .	84
Lymphangitis (Allosan) 87; (Ichthyol) . . . . .	216
Lymphatic gland sarcoma (Sod. cacodyl.) . . . . .	10
Lymphoma (Iodo-guaiacol) . . . . .	202
Malaria (Sod. cacodyl.) 16; (Ferri cacodyl.) 32; (Quinine) 297; (Cholesterin) 144; (Enesol) 173; (Medulla) 270; (Salvarsan) . . . . .	308
Malarial cachexia (Sod. cacodyl.) . . . . .	16
» gastralgia (Sod. cacodyl.) . . . . .	16
Mallenders (Scarlet Red) . . . . .	324

	Page
Mammary carcinoma (Antituman) 97; (Substitol) . . . . .	356
Mastitis (Alcohol) . . . . .	84
Measles (Calc. sulphide) . . . . .	135
Melæna (Gelatina steril.) . . . . .	191
Melancholia (Sod. cacodyl.) 25; (Bornyval) . . . . .	129
Meningitis cerebrospinalis (Perhydrol) 280; (Serum) 335; (Urotropine) . . . . .	368
Menorrhagia (Atropine) . . . . .	120
Menstruation, anomalies of (Bornyval) 129; (Eumenol) 176; (Corporalutea) 263; (Stypticin) . . . . .	354
Metritis (Fibrolisin) 185; (Stypticin) 354; (Thilaven) . . . . .	361
Metrorrhagia (Atropine) . . . . .	120
Migraine (Sod. cacodyl.) 26; (Pyramidon) . . . . .	295
Mitral insufficiency (Bornyval) . . . . .	129
Morphinism (Dionin) 167; (Scopolamine) . . . . .	328
Muscular rheumatism (Diplosal) 170; (Kephaldol) . . . . .	235
Myalgia (Diplosal) . . . . .	170
Mycosis fungoides (Sod. cacodylic.) . . . . .	10. 14
Myocarditis (Bromural) 132; (Nitroglycerin) 251; (Periplocin) . . . . .	283
Marginal phlyctenules (Hydrarg. biniod.) . . . . .	211
Nævi (Pot. permangan.) 288; (Carbonic acid.) . . . . .	241
Nasal hæmorrhage (Calc. lactas.) 133; (Digitalis) . . . . .	157
» vet. (Adrenalin) . . . . .	77
Nasal syphilis (Hydrarg. metall.) . . . . .	213
Neck, syphilis of the (Hydrarg. metall.) . . . . .	213
Nervous diseases (Sod. cacodyl.) 25; (Bromural) . . . . .	132
Neuralgia (Acid. cacodylic.) 9; (Alcohol) 84; (Bromipin) 131; (Gynoval) 203; (Kephaldol) . . . . .	235
Neurasthenia (Sod. cacodyl.) 11; 25; (Hydrarg. cacodylic.) 35;	

	Page		Page
(Kephir) 52; (Arsentriferrin) 111; (Bromipin) 131; (Bromural) 132; (Cholesterin) 145; (Gynoval) 203; (Novaspirin) 255; Physostigmine) 285; (Sabromin) 301; (Valisan) . . .	368	Peritonitis (Acid. nuclein.) 70; (Adrenalin) 76; (Camphora) 135; (Leucofermantin) . . .	238
Neuritis (Strychnine) . . .	353	» tuberculosa (Sod. cacodyl.) 23; (Borinyval) . . .	129
» toxica (Pyramidon) . . .	294	Pertussis (Kephir) 54; (Aris-tochin) 107; (Bromipin) 131; (Quinine) 297; (Gomenol) 197; (Iodine) . . . . .	222
Neuroses (Gynoval) 203; (Sod. cacodyl.) . . . . .	344	Petechial fever (Iodipin) . . .	226
Obesity (Iron Sajodin) . . .	233	Pharyngitis (Iodo-guaiacol) . .	202
Oesophageal stricture (Fibro-lysin) . . . . .	183	Phlebitis (Alcohol) . . . . .	84
Omarthritis (Fibrolysin) . . .	181	Phlyctenules (Argyrol) 106; (Hydrarg. biniod.) . . . . .	211
Oöphoritis (Fibrolysin) 185; (Thilaven) . . . . .	361	Phosphaturia (Sod. cacodyl.) . .	26
Ophthalmia, gonorrhœal (Argent. acet.) 100; (Argyrol) 105; (Perhydrol) 281; (Sophol) 350		Pityriasis rosea (Sulphoform) . .	359
» granulosa (Acid. boric.) . . .	66	Placenta prævia (Atropine) . . .	120
» neonatorum (Acid. picric.) 72; (Argent. acet.) 100; (Lenicet) 235; (Perhydrol) 281; (Sophol) . . . . .	281	Plague (Adrenalin) . . . . .	76
Optic nerve atrophy (Iodival) .	227	Pleurisy (Iodival) 227; (Naph-thol) 252; (Diplosal) . . . . .	170
Osteo-arthritis (Sod. cacodyl.) . .	18	» , with effusion (Adrenalin) 76; (Diplosal) 170; (Hy-dropryrene) . . . . .	216
Osteomalacia (Adrenalin) 76; (Iodival) . . . . .	227	Pneumonia (Collargol) 105; (Digitalis) 159; (Digipuratum) 161; (Digitoxin) 163; (Strych-nine) . . . . .	353
Ostitis tuberculosa (Sod. cacodyl.)	18	Polyarthritis chron. (Fibrolysin) 182	
Oxyuris (Oleum Chenopod.) . . .	260	Poliomyelitis (Perhydrol) . . .	281
Pachydermia (Eugallol) . . . . .	176	Post-partum hæmorrhage (Atro-pine) . . . . .	120
Paludism (Sodium monomethyl-arsen.) . . . . .	37	Pott's disease (Sod. cacodyl.) . .	17
Papilloma (Pot. permangan.) . .	288	Pretuberculosis (Sod. cacodyl.)	12
Paralysis (Acid. nucleinic.) 69; (Salvarsan) . . . . .	308	Proctitis (Kaolin) . . . . .	127
» agitans (Hypophysis) . . . .	269	Prostatitis (Allosan) . . . . .	87
» spasmodica (Fibrolysin) . . .	182	Pruritus (Coryfin) . . . . .	150
» vet. (Yohimbine) . . . . .	373	» ani (Anthrasol) . . . . .	93
Parametritis (Iron Sajodin) 233; (Thilaven) . . . . .	361	» universalis (Anthrasol) . . .	93
» actinomycotic (Iodipin) . . .	223	» vulvæ (Anthrasol) . . . . .	93
Pemphigus (Quinine) . . . . .	296	Pseudoleukæmia (Sod. cacodyl.) 10; (Arsacetin) . . . . .	108
Perichondritis tuberculosa (Co-ryfin) . . . . .	151	Psoriasis (Sod. cacodyl.) 10; 13; 14; 344; (Hydrarg. iodocaco-dyl.) 35; (Anthrasol) 93; (Arsacetin) 110; (Chrysarobin) 147; (Salvarsan) . . . . .	308
Perimetritis (Thilaven) . . . . .	361	Psychoses (Acid. nuclein.) 70; (Physostigmine) 285; (Veronal) 371	
Periostitis (Iothion) . . . . .	231		



	Page
Puerperal infection (Collargol)	
104; (Digipuratum)	161
Pyodermatitis (Ichthyol)	217
Pyrosis (Magnesium-Perhydrol)	245
Pyorrhœa alveolaris (Para-mono-	
chlorphenol) 276; (Perhy-	
drol)	278
Radical operation on the mas-	
toid process (Carbo)	138
Reagents and Reactions: 64.	
72. 77. 92. 95. 99. 120. 140.	
152. 155. 162. 165. 166. 189.	
213. 218. 246. 250. 252. 261.	
282. 289. 295. 301. 346. 348.	
357. 361. 366.	375
Rectal abscess (Kaolin)	127
Rectum, carcinoma of the (Anti-	
tuman)	96
» stricture of the (Fibro-	
lysin)	183
Recurrent fever (Arsacetin) 109;	
(Atoxyl) 115; (Salvarsan)	308
Remittent fever (Acid. cacodyl.)	8
Retinal detachment (Dionin)	169
» hæmorrhage (Dionin)	168
Retroversio uteri (Fibrolysin)	186
Rheumatism (Kephir) 52; (Ad-	
renochrom) 77; (Alcohol)	
84; (Diplosal) 170; (Iodi-	
pin) 224; (Spirosal)	350
» , articular (Diplosal) 170;	
(Hydropyrine)	216
» chron. (Fibrolysin) 181;	
(Streptoc. Serum)	335
Rhinitis (Kaolin) 127; (Coryfin)	
150; (Menthol)	249
Rib contusions (Alcohol)	84
Salpingitis (Thilaven)	361
Salpingo-œophoritis (Fibrolysin)	185
Sarcomatosis (Sod. cacodyl.)	16
Sarcoma (Sod. cacodyl.)	16
Scabies (Anthrasol)	93
Scar formation (Fibrolysin)	181
Scarlet fever (Kephir) 54; (Calc.	
sulphide)	135
Scars (Fibrolysin)	183

	Page
Sciatica (Sod. cacodyl.) 25; (Co-	
caine) 149; (Fibrolysin)	182
Scleral tuberculosis (Acid. lact.)	69
Scleritis (Dionin)	169
Scleroderma (Fibrolysin) 184;	
(Iodo-guaiacol) 202;	
(Gland. Thyroid.)	268
» vet. (Iothion)	231
Scrofula (Sod. cacodyl.) 11;	
(Kephir) 52; (Arsentriferrin)	
111; (Iron Sajodin)	233
Scurvy (Alsol) 89; (Perhydrol)	208
Sea sickness (Bromural) 132;	
(Veronal) 372; (Veronal-So-	
dium)	373
Senile cataract (Lentocalin)	270
Sepsis (Streptoc. Serum)	336
Shock (Hypophysis)	269
Skin disinfect. (Ethylen. chlor.)	
83; (Alcohol) 85; (Anti-	
formin) 95; (Benzene) 123;	
(Chlor-meta-kresol) 141;	
(Iodogomenol) 197; (Iodine)	
219; (Iothion)	231
» diseases (Acid. cacodyl.) 7;	
9; (Sod. cacodyl.) 13;	
(Kephir) 52; (Afridol) 84;	
(Alumin. acet. tartar.) 88;	
(Anthrasol) 93; (Arsen-	
triferrin) 111; (Quinine)	
296; (Iodo-guaiacol) 202;	
(Sulphoform) 358; (Zinc-	
Perhydrol)	379
» , infiltrated (Resorcin)	300
» sarcomatosis (Sod. cacodyl.)	10
» thickening, vet. (Fibro-	
lysin)	188
» tuberculosis (Sod. cacodyl.)	10
Small intestine, catarrh of the	
(Protargol) 292; (Taka-dias-	
tase)	360
Spondylitis (Bismuth subnit.)	124
Starch dyspepsia (Taka-dias-	
tase)	359
Stomatitis (Iodo-guaiacol) 202;	
(Iothion) 231; (Perhydrol)	280
» aphthosa (Alsol)	89
» mercurialis (Alsol)	89

	Page		Page
Struma (Sod. cacodyl.) 26; (Antithyroidin) . . . . .	330	Tonsillitis lacunaris (Pyocyanase)	293
Suppuration (Amidoazotoluol) 91; (Bismuth. subnitr.) 123; (Kaolin) 127; (Carbo) 138; (Leucofermantin) 236; (Resorcin) . . . . .	300	Toothache (Novaspirin) . . .	255
Swallowing, difficulty in (Pyramidon) . . . . .	294	Tooth, caries (Monochlorphenol) 276 » treatment of roots (Monochlorphenol) . . . . .	276
Synovitis (Fibrolysin) . . .	182	Trachoma (Acid. boric.) 66; (Acid. picric.) 72; (Collargol)	104
Syphilis (Sod. cacodyl.) 11; 15; 343; (Hydrarg. cacodyl.) 33; (Hydrarg. iodocacodyl.) 34; (Arsacetin) 107; (Asurol) 112; (Atoxyl) 115; (Atoxyl-mercury) 117; (Enesol) 172; (Fibrolysin) 187; (Hectin) 203; (Hydrarg. benzoas) 209; (Hydrarg. metall.) 212; (Hydrarg. oxycyanid.) 214; (Hydrarg. salicylic.) 215; (Iodo-glidine) 227; (Iodipin) 224; (Iodival) 226; (Iothion) 229; (Pot. bichrom.) 286; (Mergal) 249; (Sajodin) 303; (Salvarsan) 304; (Scarlet Red) . . .	324	Trigeminal neuralgia (Alcohol)	85
» , vet. (Sod. cacodyl.) . . .	28	Trypanosomiasis (Sod. cacodyl.) 16; (Arsacetin) 109; (Arsenophenylglycin) 110; (Quinine)	298
» diagnosis (Sod. glycochol.) 347; (Dungern's test) 340; (Cuorin) . . . . .	151	Tuberculosis (Sod. cacodyl.) 10; 18; (Guaiacol cacodyl.) 32; (Strychnine cacodyl.) 36; (Sod. monomethylarsen.) 37; (Carbenzyme) 137; (Cholesterin) 145; (Gomenol) 196; (Limonene) 239; (Menthol) 248; (Hypophysis) 269; (Ovaria) 271; (Tuberculin) 338; (Tuberculo) 338; (Trypsin) . . .	365
Tabes dorsalis (Fibrolysin) . .	185	Tumours (Calc. sulphur.) 135; (Carbenzyme) 137; (Leucofermantin) 238; (Substitol)	355
Tapeworm (Filmaron) 188; (Kamala) . . . . .	234	» fibrous (Fibrolysin) . . .	188
Teeth, bleaching of (Perhydrol) 280 » bleeding (Gelatina steril.) 192		Tympanic membrane, perforation of (Acid. picric.) . . . . .	72
Telangiectasis (Carbonic acid.) 241		Typhoid fever (Aristochin) 106; (Calc. sulph.) 135; (Hordenin) 209; (Kephaldol) 235; (Oleum terebinth.) 260; (Medulla) 270; (Pyramidon) 293; (Serum)	339
Tendinitis fibrosa (Fibrolysin) .	188	Ulcers (Pot. permangan.) 288; (Pergenol) 277; (Scarlet Red) 324; (Zinc-Perhydrol) . . .	378
Tetany (Magnes. chlor.) 243; (Magnes. sulph.) 243; (Gland. Parathyr.) . . . . .	263	Ulcus molle (Protargol) 292; (Pyocyanase) 293; (Scarlet Red) 323; (Zinc-Perhydrol) . . . . .	379
Tetanus, vet. (Iodipin) . . . .	224	» rodens (Carbonic acid) . . .	241
Tongue, epithelioma of the (Sod. cacodyl.) . . . . .	16	» serpens corneæ (Collargol) 104; (Dionin) 169; (Europhen) . . . . .	178
Tonsillitis (Alcohol) 84; (Iodoguaiacol) 202; (Perhydrol) 280		» ventriculi (Atropine) . . .	120
		Urethritis catarrhalis (Allosan)	87
		Urethro-vaginitis infantum (Isoform) . . . . .	232

	Page		Page
Urticaria (Fæx) 181; (Hydro- pyrine) . . . . .	216	Warts (Liq. calc.) 241; (Car- bonic acid.) . . . . .	241
Uterus atony (Hypophysis) .	269	Whitlow (Alcohol) 84; (Ar- gent. nitric.) 102; (Pot. per- mangan.) . . . . .	287
» fixation (Fibrolysin) .	185	Whooping cough, (Aristochin) 107; (Bromipin) 131; (Quinine) 297; (Gomenol) 197; (Iodine) 222	
» carcinoma (Acetone) 64; (Antituman) 97; (Zinco- pyrin) . . . . .	377	Women, diseases of . . . . .	185
» , displaced (Fibrolysin) .	185	Wounds (Amido-azotoluol) 91; (Antipyrine) 95; (Argent. nitr.) 101; (Carbo) 138; (Cyclo- form) 154; (Iodine) 219; (Mastich) 247; (Novoiodin) 258; (Pergenol) 277; (Per- hydrol) 284; (Salol) 304; (Scarlet Red) 324; (Zinc- Perhydrol) . . . . .	379
Vaginal discharge (Kaolin) .	127		
Vaginitis (Novoiodin) . . .	258		
Variola (Pot. permangan.) 288; (Salvarsan) . . . . .	308		
Vascular neuroses (Bromural) .	132		
Verruca plana (Liq. calc.) . .	241		
Vitreous, hæmorrhage (Fibro- lysin) . . . . .	186		
Vulvo-vaginitis (Kaolin) . . .	128		



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